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XLIII

# TRAUMATIC STRICTURE OF THE LARYNX

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Laryngeal injuries, although uncommon in peace time, are becoming increasingly more important because of the increased accident rate from the greater number of cars, and with higher horsepower, crowding the roads. I would like to show that with improved treatment of these cases, the previous high mortality and morbidity can be reduced. A wide variety of accidents, in addition to motor vehicle accidents, have been implicated: stab-wounds; hanging; strangulation; a blow struck by fist, elbow, knee or ball in athletic events, and various industrial accidents. Damage resulting in stenosis may result from irradiation or acute or chronic inflammation, high tracheotomy or endotracheal anesthesia. Lederer[8] called attention to the increase in laryngeal injuries during World War II, not only from gunshot and shrapnel, but also from the use of Judo. The condition was first mentioned by Morgagni but the first accurate description was given by Gurlt[18] in 1884. The relative infrequency of laryngeal injury is due to the protected position of the larynx with the mandible, sternum, and clavicles acting as bumpers; and also because of its mobility and resiliency the larynx can "roll with the blow." This is an important current subject since mortality up to 75 per cent has been ascribed to laryngeal fractures,[6] and mismanagement is common. As might be expected, these cases do not immediately come to the attention of those best qualified to care for them. They are first seen by general doctors, or appear in emergency rooms and general surgical wards where the potentially serious nature of the injury is frequently

unrecognized, and supportive care is given while valuable time is lost in preventing prolonged disability.

The mildest type of injury is contusion of the neck and larynx with submucosal hematoma.[12] Nach and Rothman[11] describe "subcutaneous rupture," apparently meaning tracheal or laryngeal mucosal tear without skin laceration and accompanied by emphysema, caused by sudden neck extension or cough increasing the intrathoracic pressure. Laryngeal injuries may be classified as contused, lacerated, incised, penetrating, or crushing.[9] The age at which the laryngeal cartilages calcify and later ossify varies, but calcification usually commences about the twenty-fifth year.

The type of laryngeal fracture occurring may be simple or comminuted, oblique, vertical, or irregular. The thyroid ala may be compressed laterally. Fracture of the cricoid is associated with more severe injuries with associated blood vessel and vagus injury and a high mortality. The arytenoids may be dislocated, usually with the tip leaning anteriorly obstructing the larynx and permitting relaxation of the cords. Edema and submucosal hemorrhage may be severe and constrict the airway. The epiglottis may be partially severed at its base and obstructive. Subcutaneous and mediastinal emphysema may be alarming. Later scar tissue contracture occurs and a slowly progressive dyspnea may occur. Kernan[7] cites the occasional very slow response of the larynx to injury, at times taking years to show its full effect in the production of dense scar tissue. Lynch[9,14] reports three cases of carcinoma probably from epithelial cells carried into penetration gunshot wounds.

Baily classifies several anatomical sites of injury: 1) wounds above the hyoid, 2) wounds of thyrohyoid membrane, 3) wounds of thyroid cartilage, 4) wounds about the cricoid, and 5) tracheal wounds. Varying degrees of anoxia and hemorrhage may be present.

Shock and loss of consciousness may appear out of proportion to the apparent mildness of the injury. In considering the prognosis each case is considered serious and judgment reserved as to final outcome. Sudden death from asphyxia has been reported a number of times.

The complications are aspiration, perichondritis, and chondritis, pneumonia, emphysema, and hemorrhage. The last is less apt to occur in high wounds because the large vessels are deeper here. The signs and symptoms are pain over the neck and on swallowing, tenderness, swelling, hoarseness, stridor, cough, cyanosis, wheezing, aphonia,

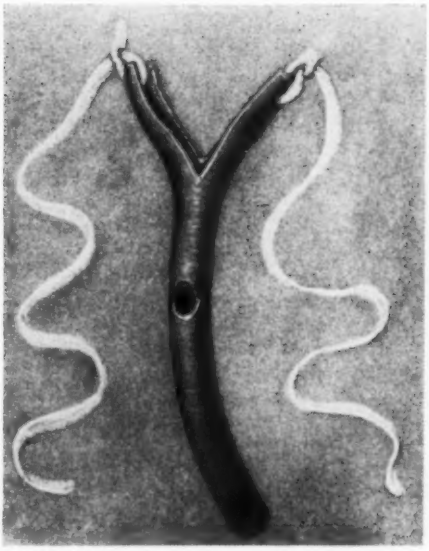

Fig. 1.—Tracheotomy cannula that may be improvised from a piece of rubber tubing. (After Nach and Rothman,[11] by permission Surgery, Gynecology and Obstetrics)

bloody expectoration, dyspnea with retraction of the suprasternal notch, and subcutaneous emphysema. If an external laceration is present there may be an audible escape of air and bloody bubbles. If the hyoid is fractured there is pain on protrusion of the tongue. Laryngeal examination reveals swollen violaceous mucosa. The diagnosis is established by the history, the swollen, ecchymotic and tender neck, and the other findings above. Direct laryngoscopy and bronchoscopy may give additional information. The x-ray examination may show subcutaneous emphysema, abnormal contour or a foreign body. It is not of great help in demonstrating fracture lines.

Treatment is at first directed toward preservation of life by maintenance of the airway by tracheotomy or bronchoscopy. A low tracheotomy is done and may be difficult because of the marked swelling and hemorrhage. Early tracheotomy is indicated when wheezing, stridor, or dyspnea appear. In open wounds the tracheotomy tube may be temporarily placed in the laryngeal or tracheal defect. Hemorrhage is controlled by ligature or pressure. In a stab wound, with laceration of major vessels, an emergency measure that may prevent

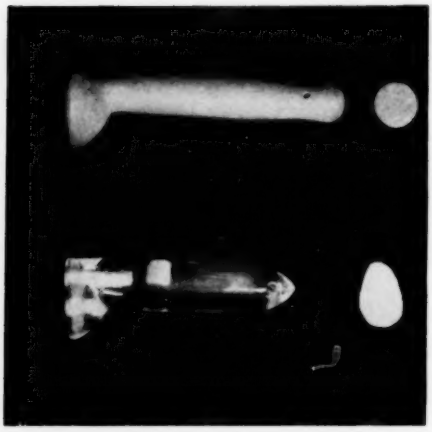

Fig. 2.—*Top*: C. Jackson's core mold. *Bottom*: Modified Luxene laryngeal splint; the head and inferior tip are perforated for introduction and anchoring to tracheotomy tube.

rapid blood loss is the insertion of the finger. Attention is next given to the treatment of shock.

The patient is hospitalized and placed at rest and asked to rest the voice. No narcotics are given because of the possibility of obstruction. Constant observation is important because sudden asphyxia may occur from hemorrhage, edema, mucous, blood clot, or detached mucosa or cartilage. Clark attended a case in which death resulted from fracture of the thyroid with a tear of mucous membrane between the true and false cords. Death occurred some time after the injury. "He is reported to have slept well during the night, but next morning about 6:30 A. M., after coughing a few times, he suddenly ceased breathing." The history shows how slight and uncertain may be the symptoms produced by a grave injury to the larynx.

Open wounds demand early exploration and careful examination to determine the possibility of blood vessel injury, the type and extent of cartilaginous fracture and the presence of a foreign body. It may be feasible at times to reduce displaced fragments and maintain stability with direct interosseous wiring. Antibiotics are important to prevent infectious pulmonary and cervical complications and perichondritis. Debridement should be minimal. As much soft tissue and cartilage as possible are retained for use in repair.

It is a problem whether the closed contused injury should be opened. There is ample opinion in the literature in favor of early operative exploration.[1,10,13] Trutner,[13] in 1942, reporting on numerous laryngeal injuries, emphasized the frequency of prolonged chondritis and perichondritis, abscess formation and foreign bodies, and advocated early surgery. It may, however, be the best plan to explore if the wound is open or if a tracheotomy is required. If an area of tenderness and swelling persists and perichondritis is suspected, incision for removal of necrotic cartilage and drainage of an abscess is better done early.

Some authors[11] advocate incisions for relief of subcutaneous emphysema, but I doubt that this is necessary. Even in the presence of alarming emphysema the fascial spaces seal in several days and swelling subsides, although there may be x-ray evidence of mediastinal emphysema. Signs of mediastinal compression are rare and if this does occur, a tracheotomy and mediastinotomy would probably be better.

If the injury is severe enough to produce dyspnea and hoarseness, early internal splinting is required. Although Chevalier Jackson's core molds have been widely used for this (Fig. 2), there is no doubt that the laryngeal mucosa of some people shows considerable reaction to the natural rubber with formation of granulations. For this reason, indwelling dilators of plastic materials patterned after these and O'Dyer's intubation tubes seem an improvement. These may be made from a model, by a dental laboratory, of an acrylic such as luxene, which is very well tolerated by the tissues (Fig. 2). They may be inserted easily through the Flagg laryngoscope with the Bennett blade (Fig. 3). They are anchored with a silk suture about the tracheotomy tube. If there is associated esophageal laceration, careful suture of mucous membrane and muscular coat in separate layers and insertion of a gastric tube is done. Gastrostomy is probably unnecessary. Levine tube feeding is used for five or six days.

Following recovery from the acute injury, there may be a progressive cicatricial stenosis necessitating tracheotomy or preventing decannulization if early tracheotomy was done. This is much less apt to occur if internal splinting was used. There may be severe hoarseness with impaired cord motility or anterior webbing. Thus one enters the stage of secondary reconstruction.

Removal of scar tissue and the use of free skin grafts in the stenotic larynx was introduced by Arbuckle in 1930. An excellent

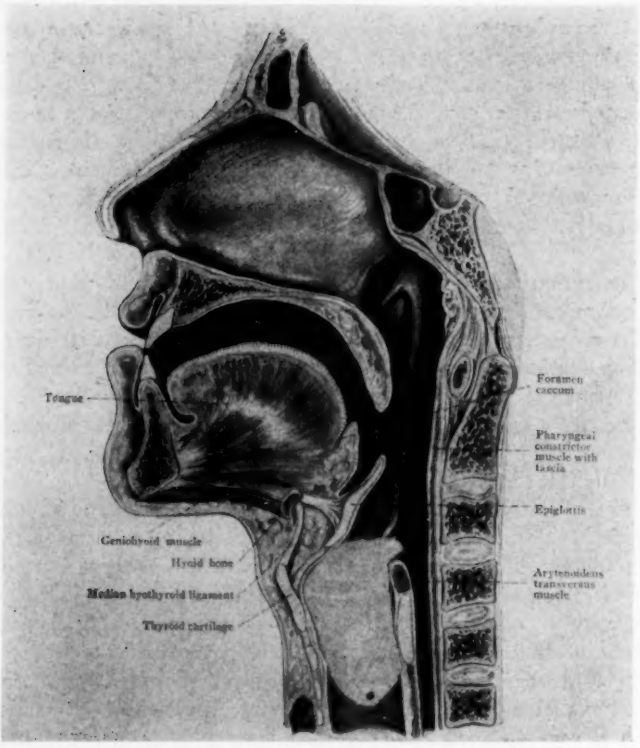


Fig. 3.—Luxene laryngeal splint in position. Note inferior perforation for anchoring splint to tracheotomy tube. (From Kirschner, Surgery of the Head and Neck, with permission of J. B. Lippincott, Publisher)

description of thyrotomy, scar excision and skin grafting over a sponge rubber cylinder is given in Figi.[17] A great advance in the elimination of anterior webbing and improving the hoarse voice was made by McNaught in the use of his ingenious tantalum keel. The psychic well being of the patient demands alleviation of as much hoarseness as possible by speech therapy.

## REPORT OF CASES

CASE 1. S.P., a colored, 20 year old Air Force M.P., while riding in a jeep at a high rate of speed struck a palm tree sustaining, among

Fig. 4.—Case 4. Note horizontal incision for exploration, internal fixation of fractures and tracheotomy. Vertical incision was necessary to remove laryngeal splint which had slipped through larynx.

other injuries, a blow to the neck. There was marked cervical swelling and tenderness and progressive dyspnea requiring tracheotomy four hours after injury. On making the initial incision, which opened an anomalous jugular venous arch, there was a violent struggle and complete respiratory obstruction. The trachea was hastily opened and a large amount of blood aspirated from trachea and bronchi. There was a postoperative left pneumothorax and aspiration pneumonia. Slow decannulization was complete after three weeks and persistent fixation of the left cord was noted.

Case 2. G.P., a 56 year old white garage mechanic, sustained lacerations of lips and tongue and contusion of the neck in an automobile accident. There was expectoration of blood and noisy, partially obstructed breathing. Examination revealed a transverse laceration of the base of the epiglottis so that it overhung the larynx, producing obstruction. There was also unilateral cricoarytenoid dislocation and fixation. Follow-up observation demonstrated permanent hoarseness.

Case 3. T.B., a 14 year old white boy, in an auto accident, struck the front of his neck against the dash board. There was marked tenderness and swelling and immediate hoarseness. He was treated by his doctor with bed rest. Progressive laryngeal obstruction over the next week was regarded as hysteria and when the patient was seen by the author he was in extremis. A low tracheotomy was done.

Examination revealed a great mucosal swelling nearly obliterating the lumen. After several days a core mold was introduced, and the triangular laryngeal dilators were used at the time of changing core molds to larger sizes over a period of six months before extubation could be accomplished successfully. At present there is mild hoarseness and no dyspnea on exertion. There is slight anterior webbing.

CASE 4. A.B., a 35 year old white woman, struck her neck in an automobile accident. Cervical subcutaneous emphysema, tenderness, and ecchymosis and mild inspiratory stridor was noted. After three days of observation an increase in dyspnea occurred and a tracheotomy and internal splinting with a plastic core mold were done. Examination revealed bilateral violaceous swelling about the arytenoids at this time. At the time of tracheotomy a laryngofissure was done. There was tremendous thickening of the cricothyroid membrane. A vertical and intersecting oblique fracture line was found. An unsuccessful attempt to reduce an anterior crico-arytenoid dislocation was made. Direct interosseous fixation of the thyroid fragments was done. The internal splint treatment was complicated by one of the core molds slipping entirely through the larynx and coming to rest on top of the tracheotomy tube. Endoscopic removal was unsuccessful, and the neck had to be reopened to retrieve the dilator (Fig. 4). Follow-up observation after decannulization revealed an adequate airway but severe hoarseness from anterior webbing and the persistently tipped and fixed arytenoid. The patient is now receiving speech therapy and considering the keel operation.

CASE 5. R.H., a 64 year old white male, had cardiac arrest while undergoing abdominal surgery. There was inadvertent removal and traumatic re-insertion of an intratracheal tube. The patient's immediate postoperative condition was precarious and four days postoperatively signs of progressive laryngeal obstruction occurred and a tracheotomy was done. Lateral cervical x-rays with soft-tissue technique showed the retrotracheal space about twice its normal width. Mirror laryngoscopy revealed great pale edematous laryngeal swelling (which subsided enough after five months to allow extubation) and a persistent fixation of the left side of the larynx, presumably traumatic cricoarytenoid ankylosis. The voice is of fair quality.

## SUMMARY

Laryngeal injuries are assuming greater importance because of automobile accidents and their high morbidity and mortality. That they are not more common is mainly because of the protected position

of the larynx. There are various types of open and closed injuries varying widely in severity. Early treatment is directed at maintaining the airway with tracheotomy, prevention of stenosis, internal splinting, and careful repair of lacerations. Later cicatricial stenosis may indicate reconstructive surgery. Rehabilitation is not complete without speech therapy for persistent hoarseness.

1838 PARKWOOD AVE.

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XLIV

# TEMPORAL AND PITCH ASPECTS OF SUPERIOR ESOPHAGEAL SPEECH

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John O. Anderson[1] in 1954 listed a bibliography of 88 items relative to esophageal speech. Since that time Robe, Moore, Andrews and Holinger[18] have contributed a major study to the field as have Bateman, Dornhurst, and Leathheart.[3] No doubt other studies are in the hands of the publishers or in progress.

The study of available source material dating from 1859 indicates a great deal of material on the incidence of cancer of the larynx and survival rate subsequent to laryngectomy,[16] the nature of the operation,[9,18] pedagogy,[2] and approximately 20 studies that agree in placing the usual locus of vibration at the level of the cricopharyngeus sphincter,[18] but which do not preclude other vibrators.[9,10] Among the more important considerations is the rather general agreement that the air-charge is usually small[22] and that for successful speakers it is taken into and expelled from the upper esophagus rather than from the stomach or lower esophagus[18] as assumed by early writers.

Generally speaking, available source materials have little to offer in the way of normative statistical information that gives direct answers to such important questions as: a) How many words and syllables can be spoken per charge of swallowed air? b) How long does it take to swallow a charge of air? c) What rate in words per minute can be achieved relative to normal speech? d) What characteristics of pitch level and variability can be anticipated in esophageal speech?

It is the purpose of this study to describe the time and pitch performances of six superior esophageal speakers utilizing speech sam-

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ples of adequate length for which norms for rate,[5] breathing,[21] and pitch[6] are already available for normal or superior speakers.

## SELECTION OF SUBJECTS

Superior speakers were selected so that any generalizations arrived at might serve as suitable goals for those learning to speak without a larynx.

An initial group of 52 satisfactory performers from Southern California was obtained through contact with otolaryngologists, speech therapists, the Veterans' Administration, the American Cancer Society, the Lost Chord Club of Los Angeles, and the New Voice Club of San Diego. The senior author screened this group successively to 23 and finally to ten performers. At this stage the following passage from Fairbanks[7] was recorded for each of the ten performers:

"When the sunlight strikes raindrops in the air, they act like a prism and form a rainbow. The rainbow is a division of white light into many beautiful colors. These take the shape of a long round arch, with its path high above, and its two ends apparently beyond the horizon."

These ten recordings were presented, when necessary, by mail, to eight skilled and experienced judges, and included the following directions:

"Please number your papers from one to ten.

"You will presently hear ten brief readings of esophageal speech. These recordings have already been screened for general effectiveness from 23 performances which in turn were screened from 52 performances. This indicates that all of the final samples are reasonably effective for the type of speech under consideration.

"Please rate each speaker for general effectiveness on a one to five rating scale. One equals poor, two equals fair, three equals average, four equals good, and five equals excellent. Judge on these samples only, not on other samples of speech that you have heard.

"A brief word about general effectiveness. Its first attribute is intelligibility, but consideration is also given to those attributes of rate, loudness, pitch, quality, and articulation that make the content easy to assimilate without stress or discomfort on the part of the speaker.

"Do *not* penalize for misreading or mispronunciation.

"You will hear all performances through once before being asked to judge. Record your judgments only on the second playing of the record."

On the basis of these judgments six speakers were selected and utilized for the pitch study. Because of the serious illness of one speaker the next ranking speaker was chosen for the six speakers used for the duration measurements.

All of the speakers were males with at least four years of experience with esophageal speech. Three of the speakers were experienced teachers of esophageal speech. There were excellent female speakers in the original group, but none appeared to match the performance of the male subjects who were finally selected. Six judges were requested to select female voices from the male voices on the basis of recordings alone. Their complete lack of success tends to indicate marked similarity in the voices of male and female esophageal speakers.

Each of the six speakers performed at the highest level of esophageal speech as defined by Wepman, MacGahan, Richard, and Shelton.[23] In other words they spoke with continuity and without consciousness of the act of swallowing and eructation. The speech was easily and naturally produced without apparent thought or effort.

## EXPERIMENTAL PROCEDURE

The air-charges were recorded by means of a sensitive light weight electropneumograph placed high on the chest and similar in design and construction to that previously described by Snidecor[21] for the recording of the breathing cycle for superior speakers. In this present study an intensity modulated 1,000 cycle tone served as an air-charge signal and was recorded on one channel of a dual channel magnetic tape recorder while speech was being recorded on the other channel. At a later time the information on each channel was transferred to the moving photographic tape of a Miller Light Writer traveling at 45 mm per second which supplied a visual record of "breathing" and speech that was amenable to measurements. The electrical and photographic means of achieving this final record can best be described by schematic drawings which are available from the senior author. The rise in esophageal air pressure which actuated the pneumograph is described by Bateman, Dornhurst, and Leathheart[3]

as ". . . always accompanied by a sharp expiratory effort and loss of air from the lungs." This puff of air was audible and served to check the electrical recording. The writers believe that the recording of this puff might serve as an economical and reasonably accurate index of air-charge where it appeared desirable to make time estimates based on larger samples of speech.

As described under "Selection of Subjects," each subject recorded a portion of the Rainbow Passage.[7] This passage was used in selecting the subjects, and also for phonelloscopic analysis. All pitch data herein discussed are from this selection.

While recording both his voice and air-charges each speaker performed "as if speaking to an audience of 25 people." First, the subjects were requested to count to ten as many times as possible on one air-charge. The best of three trials was selected for study. Counting is commonly practiced and demonstrated by esophageal speakers. It will be noted that the count to ten requires the speaking of eleven syllables. Second, each subject read and was recorded for the Rainbow Passage[7] attempting to "breathe" at points he had marked as representing his best spots to pause for air. This performance can be dismissed briefly, but not thoughtlessly, by noting that these skilled speakers did not predict with any degree of success when they were going to take an air-charge. Those learning esophageal speech frequently mark passages and take air accordingly. Their skilled counterparts are no more conscious of air intake than normal conversational speakers. Third, each subject read the "Rate Passage"[7] with a break for rest at the end of the first paragraph. From 43 to 48 air charges from this passage were studied for each subject. All temporal data except counting are based on the results from this passage, a sample of which is presented later in this paper.

All temporal measurements were made directly from the photographic record with a simple analogue computer that read directly in seconds and decimals thereof. These results were checked against a one-tenth of a second time line recorded on the photographic tape.

Using the phonophotographic technique originated by Metfessel,[14] modified by Simon[19] and Lewis and Tiffin[12] and electrified by Cowan,[4] pitch curves were plotted from frequency measurements, and measures of pitch were computed.

On the apparatus used for this study, the recording drum circumference was 191.2 cm; the temporal extent of each measurement interval was 0.051 sec.

EXPERIMENTAL RESULTS, RATE

One of the best general measures of efficiency in speech is rate. Darley[5] established norms for the passage in question for normal speakers and found that the zero percentile was represented by 129 words per minute, the fiftieth percentile by 166 words per minute, and the one hundredth percentile by 222 words per minute. Franke[8] in an investigation of the judgment of rate found that critical listeners found rate too rapid if it exceeded 185 words per minute or too slow if it was less than 140 words per minute.

Perusal of Table I, Item 1 indicates that these superior esophageal speakers ranged from 85 words per minute to 129 words per minute for an extended performance. For the brief, 56 word "Rainbow Passage" speaking rate was somewhat more rapid than for the long passage. The range was from 108 to 137 words per minute with a median rate of 122.5. No speaker exceeded Darley's fifth percentile, nor did any speaker achieve a rate that would have been judged adequately rapid in terms of Franke's data. One hundred and twenty words per minute, or two words per second, is the rate at which efficient secretaries take shorthand. This rate is not slow enough to disturb the average listener. Too much should not be made of rate, for speaker Number three, Table I, was consistently judged as superior to speakers four, five, and six, yet his rate of 85 words per minute was considerably lower than the rates 109 words per minute, 120 words per minute, and 129 words per minute for these speakers.

The question obviously arises: can the esophageal speaker speed up his rate? The answer is that he can do so only within narrow limits without sacrifice of loudness or suitable phrasing. This fact was borne out by trial runs for more rapid rate which were largely unsuccessful. This lack of modifiability is readily explained by the need for frequent air-charges on the part of even highly efficient esophageal speakers.

Item 2 in Table I, that of counting, gives some idea of this problem as will further information in Table I. None of the six speakers exceeded the count of ten (11 syllables) in the three trials allowed each speaker. Speaker number five insisted that he could count to at least thirty without an air-charge. The electropneumograph proved that small air-charges were taken after the count of ten. This speaker was completely unconscious of this fact until he saw evidence of the air-charges on the instrument following the experimental run. It will be noted, however, that speaker five did read as high as 22 syllables on one air-charge, a figure exactly equal to the count of ten repeated

TABLE I

TEMPORAL RELATIONSHIPS

| SPEAKER NUMBER | 1 | 2 | 3 | 4 | 5 | 6 | SUPERIOR "NORMAL" SPEAKER |
|---|---|---|---|---|---|---|---|
| 1. Words per minute | 120 | 114 | 85 | 109 | 120 | 129 | 140 to 185 |
| 2. Count, best of three trials | 10 | 8 | 10 | 4 | 10 | 7 | 40 (estimate) |
| 3. Mean words per air-charge | 4.2 | 5.2 | 2.8 | 2.9 | 6.3 | 3.5 | 12.5 |
| 4. Range in words per air-charge | 1-10 | 1-10 | 1-5 | 1-5 | 3-15 | 1-8 | 2-36 |
| 5. Sigma, words per air-charge | 1.8 | 1.9 | 1.0 | 1.0 | 3.0 | 1.4 | 4.9 |
| 6. Mean syllables per air-charge | 5.8 | 7.6 | 3.9 | 3.8 | 8.7 | 5.2 | 17.5 (estimate) |
| 7. Range in syllables per air-charge | 3-12 | 2-13 | 2-6 | 1-7 | 4-22 | 2-11 | 2-50 (estimate) |
| 8. Sigma, syllables per air-charge | 2.11 | 2.57 | 1.13 | 1.21 | 4.05 | 1.95 | No data |
| 9. Mean pause time for air-charge | .54 | .76 | .63 | .42 | .80 | .64 | .75 to .94 |
| 10. Mean duration of air-charge | 1.54 | 1.75 | 1.04 | 1.00 | 2.25 | 1.25 | 4.19 |
| 11. Mean pause time for phrases | .72 | 1.13 | 1.05 | .62 | 1.06 | .76 | .63 |

twice which contains 22 syllables due to the two syllables in the digit seven.

These and following data must be interpreted in relationship to the experimental situation lest the results be challenged by those[11] who insist that advanced esophageal speakers produce 200 syllables with one mouthful of air, and that they can count to 70 on one "breath." The esophageal speakers in this study were held to a loudness level suitable for an audience of 25 people. A check of sound level pressures indicated that they maintained these levels. Lowered intensity might well increase somewhat the number of syllables spoken. As has been stated, these superior speakers, without exception, took small charges of air efficiently and unconsciously. The superior

speaker using normal breath while reading the same passage did not begin to produce the syllables per breath claimed for some esophageal speakers.

Table I, Item 3, indicates that mean words per air-charge range from 2.8 to 6.3 for esophageal speakers with 12.5 mean words per breath for normal breathing superior speakers. The extreme range for one esophageal speaker was 15 words (22 syllables) whereas one exceptional superior speaker under identical conditions spoke 36 words (50 syllables). These differences can be shown graphically by comparing the two passages[8] below. The oblique lines in the first passage represent the air-charges taken by an efficient esophageal speaker who "charges" as frequently as most of his selected colleagues. The lines in the second passage represent the breaths taken by a superior, normal breathing speaker, who breathes as frequently as his selected colleagues.

> Your rate of speech will be adequate | if it is slow enough to provide | for clearness and comprehension, | and rapid enough to sustain interest. | Your rate is faulty if it is too rapid | to accomplish these ends. | The easiest way to begin work | on the adjustment of your speech | to an ideal rate | is to measure your present rate | in words per minute | in a fixed situation | which you can keep constant over a number of trials. | The best method | is to pick a page | of simple, factual prose | to be read. | Read this page in your natural manner, | timing yourself in seconds. | Count the number of words on the page, | divide by the number of seconds, | and multiply this result by sixty | to calculate the number of words per minute. | As you attempt to increase | or retard your rate, | repeat this procedure | from time to time, | using the same reading material, | to enable | you to check your success. |

> Your rate of speech will be adequate if it is slow enough to provide for clearness and comprehension, | and rapid enough to sustain interest. | Your rate is faulty if it is too rapid to accomplish these ends. | The easiest way to begin work on the adjustment of your speech to an ideal rate | is to measure your present rate in words per minute in a fixed situation which you can keep constant over a number of trials. | The best method is to pick a page of simple, factual prose to be read. | Read this page in your natural manner, timing yourself in seconds. | Count the number of words on the page, divide by the number of seconds, and multiply this result by sixty to calculate the number of words per minute. | As you attempt to increase or retard your rate, | repeat this procedure from time to time, | using the same reading material, to enable you to check your success. | [7]

Performance one for the esophageal speaker demanded 30 charges of air, whereas performance two for the normal speaker demanded only 11 breaths, yielding word/breath scores of 4 and 12 for the 159-word passage.

Figure 1 illustrates the performance of each group of speakers in regard to the range and mean values of words per air-charge. The

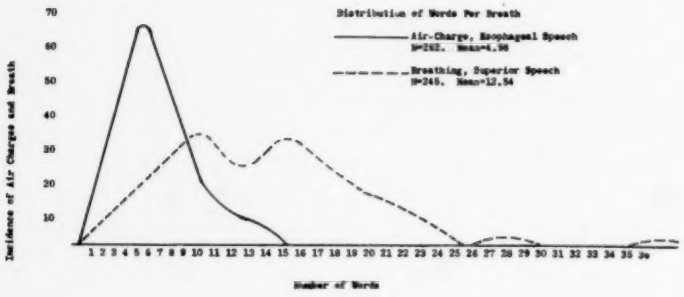
Distribution of Words Per Breath
Air-Charge, Esophageal Speech
N=282. Mean=4.98
Breathing, Superior Speech
N=248. Mean=12.54
Incidence of Air Charges and Breath
70
60
50
40
30
20
10
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
Number of Words

Figure 1

normal speaker reads aloud with an average of 12.54 words per breath, but has a wide range of performance, and tends to utilize breathing phrases of seven and fourteen words. The esophageal speaker averages 4.98 words per air-charge and has a much narrower range of performance.

Further information in Table I on syllabic performance is presented as description in addition to the grosser but more commonly used measure of words.

Our syllabic values, Item 6, are somewhat higher than those found by Stetson[22] who stated a limitation of from 3 to 4 syllables, whereas our lowest average value is 3.8 syllables, and our highest 8.7 syllables per air-charge. The number of speakers is greater in this study and also the speech sample is much larger. The Bateman, Dornhurst, and Leathheart data[3] based on three subjects and short speech samples agree with our data insofar as these are comparable. Our information, even when extreme values are considered, is far more conservative than some information given recent wide publicity.[11]

Esophageal speech despite frequent air-charges is relatively efficient and pleasant to hear. How can this be true? Table I, Item 9, answers this question in part. The skilled esophageal speakers gulped air in from .42 to .80 seconds, mean values considered. This is unbelievably rapid "breathing," fully as rapid in fact as most normal speakers breathe for speech, although it must be added that superior speakers usually breathe at phrasal limits.

If an esophageal speaker speaks at the rate of 120 words per minute, and stops for air after each five words, he would stop 24

times for one-half second or a total pause time for air of only 12 seconds in one minute. Actually he doesn't perform in such a consistent manner, for like the normal speaker he pauses for emphasis as well as breath at the ends of phrases which are defined for our purposes in this study as occurring at punctuation marks.

As indicated in Table I, Item 11, these phrase limiting pauses are markedly longer than his pauses for "breathing" alone, in fact approximately 1.41 times as long, ranging from one average of .62 to an average of 1.13. No exactly comparable figures can be stated for normal speakers, but pauses for phrases, judged as such 50 per cent or more of the time, average .63 seconds, whereas pauses infrequently judged as limiting phrases averaged only one-tenth of this value.[8] In brief, both classes of speakers pause appropriately for phrases, but it appears that the superior esophageal speaker pauses longer than the normal speaker in order that such pauses can contrast with pauses that are for air-charges only.

The value of .63 seconds for phrasal pauses for the normal speakers is shorter than the average time utilized for breathing which is probably explained by the fact that the normal speaker pauses for a number of phrases without taking a breath at these pauses.

As indicated in Item 10, the superior esophageal speaker can utilize his air-charge for approximately 1½ seconds (1.00 to 2.25) during which time he averages from 2.8 to 6.3 words. This contrasts with the normal speakers who utilize their breath for 4.19 seconds and speak 12.5 words. If relative time or words per air-charge is taken as a measure of efficiency the normal speaker is from 2½ to 3 times more efficient than the esophageal speaker.

It is probably much more reasonable to use total words per minute as a measure of efficiency and compare the average for esophageal speech of 113 words per mintue with the rate of 166 words per minute for the average normal speaker. When this is done the normal speaker speaks at only 1.47 times the rate of the esophageal speaker, or conversely the esophageal speaker is 80 per cent as fast as the average normal speaker. The fact that the esophageal speaker will always be judged as too slow[8] is of little consequence if his efficiency is relatively satisfactory, and it appears to be quite satisfactory for speech samples of 300 words.

## EXPERIMENTAL RESULTS, PITCH

Table II indicates selected measures of central tendency and variability for the frequencies recorded in the speaking performances of

TABLE II

GENERAL MEASUREMENTS OF VOCAL FREQUENCY

| | SUPERIOR ESOPHAGEAL SPEAKERS | SUPERIOR ADULT SPEAKERS |
|---|---|---|
| Median Frequency Level (c.p.s.) | 63.27 | 132.1 |
| Nearest Musical Tone | $C_2$ | $C_3$ |
| Median Frequency Level (tones above 16.35 cycles per second) | 11.70 | 18.24 |
| Mean S. D. (tones) | 2.30 | 1.88 |
| Mean Frequency Level (c.p.s.) | 62.8 | 128.1 |
| Nearest Musical Tone | $C_2$ | $C_3$ |
| Mean Frequency Level (tones above 16.35 cycles per second) | 11.65 | 17.87 |
| Mean Extent of All Inflections (tones) | 2.4 | 2.3 |
| Mean Extent of All Shifts (tones) | 2.8 | 2.6 |
| Mean Rate of Pitch Change (tone per sec.) | | |
| During Inflections | 7.9 | 17.7 |
| During Shifts | 4.3 | 7.0 |
| Mean Total Frequency Range: | | |
| Tones | 13.21 | 10.50 |
| Octaves | 2.2 | 1.75 |
| Mean Effective Frequency Range: | | |
| Tones | 6.5 | 6.3 |
| Octaves | 1.0 | 1.0 |

these superior esophageal speakers; results for the study group are contrasted with a standard set of measures on a group of selected superior normal speakers previously reported by Pronovost.[17]

The most striking feature of Table II is the difference of almost exactly one octave between the frequency levels of the superior esophageal speakers and the superior normal adult speakers, the respective median values being 63.27 and 132.1 c.p.s. These levels are very close to the musical notes of $C_2$ and $C_3$. For these carefully selected speakers, this table shows that for the superior esophageal group both the mean and median frequency used was essentially one whole octave lower than for the comparative group of superior normal speakers. This finding is graphically represented by Figure 2 which gives a distribution of the frequencies measured for the two groups of selected

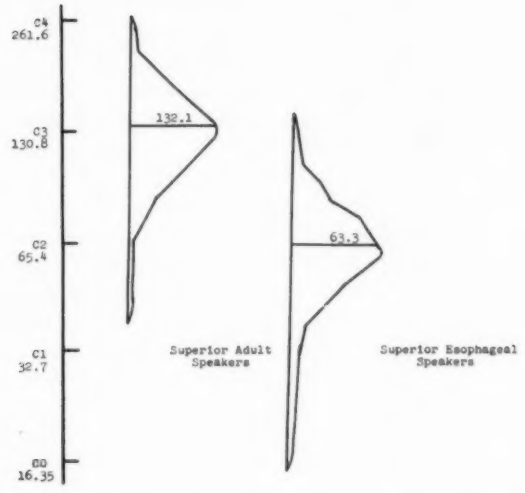


Fig. 2.—Distributions of frequencies measured for two groups of superior speakers.

superior speakers. The form of the two distributions is quite similar; the most obvious difference is, of course, the octave difference in the median frequency levels for the contrasted groups.

In addition to the difference in frequency level, the distributions of Figure 2 show a greater variability of frequency usage for the esophageal speakers than for the normal speakers. A comparison of the standard deviations presented in Table II statistically illustrates the differences. A study of the median frequency levels reported by Pronovost[17] indicates these values for the individual superior speakers of his experiment: 129.9, 116.5, 146.2, 128.8, 130.8 and 157.9 c.p.s. In contrast with these median values used by the normal speakers the highest values used by the selected superior esophageal speakers were: 115.9, 123.4, 118.7, 95.2, 112.3 and 106.6 c.p.s. Four of the esophageal speakers thus used a highest frequency which was lower than the median frequency used by the lowest of the superior normal group.

Both Table II and Figure 2 indicate the total range of frequencies used in the recorded performances; 13.2 tones for the superior esophageal speakers compared with 10.5 tones for the superior normal group. These measures exceed those reported in most previous studies for normal speakers. Lewis and Tiffin,[12] for example, found ranges

between 3.8 and 9.9 tones. According to Murray and Tiffin,[15] the frequency ranges of poor, good and trained voices are 2.9, 4.5 and 6.3 tones, respectively. For actual reading, Lynch[13] reports total frequency ranges of 5.8 tones for untrained and 8.2 tones for trained readers. The Median 90 per cent Range is somewhat more meaningful than total range and is oftimes referred to as the "Effective Range." These values are essentially the same for both groups and indicate about one octave for both superior esophageal and superior normal speakers. Again, when values for individual speakers were considered, three of the esophageal speakers exceeded the effective range for the most variable normal speaker; two values were at the same value, and only one esophageal speaker was markedly less in effective range. Table II also indicates measures for frequency and pitch movements. Group values for the mean extent of inflections and shifts are quite similar. However, the group of superior normal speakers is indicated to have considerably larger values for mean rates of pitch change. During inflections the normal group value is 17.7 tones per second while the voices of the superior esophageal group moved only 7.9 tones per second. During shifts the comparable values are 7.0 and 4.3 tones per second. These measures for rates of pitch change during inflections and shifts are, in addition to the basic difference in median frequency level, the only striking contrasts between the vocal frequency usage of the superior esophageal and superior adult speaker groups. The difference in rate of pitch change may well be a simple function operating because of marked differences in rate of speech.

## SUMMARY AND CONCLUSIONS

Utilizing a sensitive electropneumograph and phonophotographic techniques, the temporal and pitch factors in six superior esophageal speakers were studied. Major findings slightly generalized were:

1. The subjects spoke relatively easily and were no more conscious of the "breathing" function than normal speakers.

2. Three speakers counted to 4, 7, 8 respectively, and three speakers counted to 10 on one air-charge.

3. The speakers averaged five words (4.98) per air-charge, and performances averaged about 120 words per minute. A top limit of 11 to 12 syllables is very satisfactory. However, one speaker achieved an extreme range of 22 syllables.

4. The air-charge was gulped in about one-half second, a more rapid performance than that of the normal speaker inhaling for an intraphrasal breath pause.

5. The mean pitch level is almost exactly one full octave below that of the normal male speaker.

6. Pitch inflections, shifts, and total and functional pitch range are within normal limits for normal male speakers.

7. The rate of pitch change, in tones per second, is only half that of the normal speaker.

## PRACTICAL SIGNIFICANCE

This study, in exploring superior esophageal speech, with adequate samples of speech, establishes realistic norms for those who must learn to speak in this unique way. Highly efficient air-charges encompassing many syllables as reported in recent popular literature are not apparent and in our opinion are reported because the air-charge becomes unconscious for the experienced speaker. Contrary to some reports, pitch variability is comparable to that in normal speech. It is, however, very doubtful that average pitch level can be raised much, if any, above 66 to 77 cycles per second.

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XLV

# NOTES ON THE MUCOSA OF THE TRUE VOCAL CORD

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During the developmental period of organ systems in animals, patterns are usually established and followed. Various structures which are in close proximity, from the same anlage, are usually quite similar, but they may differ quite markedly in gross anatomical or histological appearance through the differentiation of physiological specialization. It is usual for the epithelium in an area and especially in a hollow viscus from the same primordium to have essentially the same cell type throughout, with minor variations which are the result of special functional requirements. The variations seen in such a hollow organ are usually quite minor, being merely an alteration of the same type of epithelium. Yet, in places where there is considerable irritation or trauma to the epithelium, the change to a more basic epithelial cell type may occur as a protective measure. In this instance the alteration in the epithelial cell type may be termed "physiological metaplasia."

When dealing with neoplasms, no stone can be left unturned in the search for causative factors. One of the first steps down the road from normal to neoplastic change in the characteristics of an epithelium is the mutation to a more primitive cell type. One of the commonest examples of this is the metaplasia due to long-standing trauma. If this metaplasia is a malignant precursor, then neoplasms should be common in certain portions of the body where metaplasia is likely.

If physiological metaplasia in an area is a predisposing factor in the production of neoplasm, then this factor should hold true in other animals in which the same change occurs, as well as in man. Later it will be discussed that physiological metaplasia from a columnar or cuboidal epithelium to a squamous cell type takes place in the mucosa covering the true vocal cords in the larynx. In view of the fact that laryngeal cancer is a relatively common disease in man (about 2 per

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cent of all neoplasms),[1] it would seem that if physiological metaplasia were a factor, this neoplasm should also appear in lower animals. Such is not the case. T. C. Jones[2] of the Armed Forces Institute of Pathology reported that in the Registry of Veterinary Pathology only two malignancies arising within the larynx could be found. One was a squamous cell carcinoma of the larynx with metastases to the lung, trachea and regional lymph nodes in a six year old male dog and the other was an adenocarcinoma of the larynx and right vocal cord with metastases to the superior cervical lymph nodes, lung, spleen and adrenal in a ten year old castrated male cat. C. F. Schlotthauer[3] of the Mayor Foundation reported: "I have collected a large series of neoplasms from various species of animals, but I have never encountered a carcinoma in the larynx in any of them. This and the trachea are the only portions of the respiratory tract in which I haven't seen a neoplasm. Carcinoma of the lungs is not uncommon in the dog. . . . I know of no reported case of carcinoma of the larynx occurring in a lower animal." William H. Feldman[4] of the same institution reported: "Personally, I have never seen such an involvement and my experience seems to be in agreement with many others who have concluded that tumor of any kind in the larynx of the lower animals is seldom seen, in fact, is indeed a rarity." W. S. Monlux of the Iowa State College Department of Veterinary Medicine stated: "Concerning laryngeal carcinoma in animals, we have found them to be very uncommon. I have never seen one. There is no record of a laryngeal carcinoma in our files. The literature I have at hand does not describe a single case." Fox,[6] in 1923, reported one case of squamous cell carcinoma in the larynx of an Azara's agouti. Others[7-15] have referred to neoplasms in the larynx and reported cases. However, as is mirrored by the paucity of material which has been found in large veterinary centers and in the veterinary literature, the larynx is an unusual location for a malignant neoplasm. Therefore, there would appear to be some other factor, phylogenetic, environmental, or habit, which is important in the production of laryngeal new growths in man as compared to lower animals.

In an effort to explain the causative factors in cancer of the throat area in man, many possible etiological factors have been hypothesized.[16] Tobacco and bidi smoking, alcoholic beverages, voice use and abuse, vitamin and dietary deficiency,[17] betel nut chewing, occupational factors, inhalation of noxious fumes, syphilis and tuberculosis have all been implicated as causative agents. Most of these are things which are peculiar to humans but not to lower animals. Man is the only animal which does any significant amount of verbalization. He is also the only one which voluntarily and habitually exposes himself

to potentially carcinogenic agents. Therefore, it would seem that the phylogenetic, environmental or habit factors are more important in the production of new growths in the larynx than is physiological metaplasia.

In most descriptions of the histology of the laryngeal mucosa it is usually stated that two different types of epithelial cells are present.[18-32] The mucosa covering the false cords, laryngeal ventricles, portions of the epiglottis and the upper trachea is usually described as ciliated columnar epithelium. The mucosa covering the true cords is usually stated to be stratified squamous epithelium. The mucosa on the posterior surface of the epiglottis and aryepiglottic folds may also be squamous epithelium. However, there is variability in the composition of the laryngeal mucosa. Lambert[33] states, "There is considerable variation in the epithelial lining of the larynx. It may consist, throughout, of an unmodified pseudostratified epithelium, with the exception of that which passes over the vocal cords; or it may consist of areas of pseudostratified epithelium alternating with areas of stratified squamous epithelium; or it may be a stratified squamous epithelium with none of the pseudostratified form appearing except in the larger ducts of the glands within the larynx. This latter condition, however, is rare. The change from the pseudostratified columnar to the stratified squamous type of epithelium is probably induced by prolonged irritation of the membrane."

To understand and explain the possible changes in the laryngeal mucosa it is important to comprehend the embryonic development of the respiratory system. The larynx in the embryo is formed in the cephalad portion of the primitive lung bud system. It develops differently in the upper and lower halves. The part above the cord folds arises from the pharyngeal floor near the primitive glottis. The lower part forms around the stem of the trachea. During the early stages of development in man and lower animals, the vocal cord is merely a rounded swelling alongside the cephalad portion of the lung bud tube. The first evidence of the lung buds appears at about the ovulation age of 21 days (17 to 20 somites) as a median thickening of the ventral wall of the foregut just cranial to the liver diverticulum. Later a pear-shaped outpouch appears on the ventral wall of the caudal end of the laryngotracheal groove. This pouch bifurcates to form the primordial lungs which first appear as two hollow projections. The respiratory portion of the foregut separates from the esophageal portion by the formation of lateral ingrowths of the surrounding mesoderm. These meet progressively and fuse in the midline in a cranial direction to form the tracheoesophageal partition. Factors

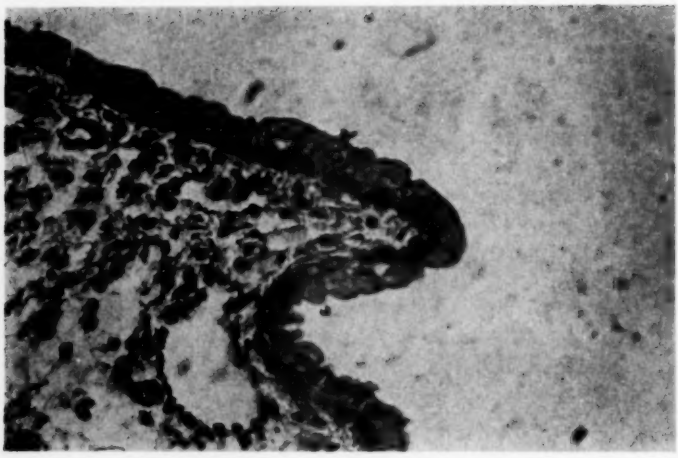

Fig. 1.—Photomicrograph (x450) of coronal section through the mid-portion of the larynx showing the mucosa covering the free edge of the true vocal cord. It is composed of definitely cuboidal shaped cells. There is no evidence of squamous metaplasia and no cilia.

which prevent normal formation of the lungs must become effective not later than early in the second month of menstrual age.[34] During the fourth week a transverse ridge, the epiglottis, appears immediately caudal to the tongue.[35] This structure joins the arytenoid swellings at the upper end of the laryngeal groove forming a U-shaped ridge, called the furcula. At this period in the embryonic development the glottis assumes a "T" shape and soon becomes closed temporarily by fusion of the epithelium. At eight weeks the laryngeal ventricles are solid epithelial outgrowths. The larynx opens at about ten weeks, having an oval shape. From this point until birth, the changes in the larynx are primarily those of development of the cartilagenous framework, the musculature, nerves and the connective tissue elements. The larynx develops in a cephalad direction and as a result, in the fetus and newborn it lies higher than in the postnatal period.[36-43]

The lungs develop by elongation of the trachea, the bifurcation into the primary lung buds and secondary bifurcation into the various lobes. The epithelium of the trachea and bronchial tree is a continuation of that from the evagination from the primitive foregut.[44-45] According to Stewart,[46] the tracheobronchial epithelium in the em-

bryo is of a tall columnar or cuboidal type. This becomes flattened with the first respiratory efforts.

Assuming that the mucosa of the larynx follows the pattern of the remainder of the respiratory tract it could be expected that a columnar or cuboidal, possibly ciliated, epithelium would appear in some embryonic stage of development. If this be true, then the stratified squamous epithelium found in the individual after birth would be a physiological metaplasia. This possibility was mentioned by Grant[47] who noted that the larynx has ciliated stratified epithelium which gives way to nonciliated epithelium where vibration and impact occurs, primarily over the vocal folds and the epiglottis. This same effect on the mucosal pattern of the larynx was attributed to "attrition" by Baily.[48]

Kiebel,[49] in 1912, stated regarding the laryngeal mucosa, "The distinct delineation of the vocal cords first occurs, however, in the middle of the third month (fetus of 37 mm according to Soulie and Bardier); their epithelium differs from that of the surrounding regions after the stages of 45 to 50 mm by the absence of cilia. . . . Yet, at birth the free edge of the vocal cord is rounded and only assumes its definitive form within the first six months of extra-uterine life. . . . The central epithelium with which they are covered is replaced by a squamous epithelium in the course of the first year."

More recently, Hopp[50] examined the mucosa of the larynx in fetuses and noted that there was evidence of physiological metaplasia from a columnar or cuboidal epithelium over the true cords in the embryo to a squamous epithelium at birth. Bianchi,[51] Berendes,[52] and Walander[53] have also presented discussions of the larynx in the fetus with similar findings. However, Valadez[54] reported three fetal larynxes in cross section, two of 18 weeks' gestation, born dead, and one of 25 weeks' gestation which lived for 43 hours. The epithelium was reported as "most of the lining is of stratified squamous epithelium." These somewhat controversial findings raise the question as to whether the physiological metaplasia of the laryngeal mucosa occurs during the intra-uterine life by means of stretching motions of the cords with flattening of the mucosa, or after the child is born.

Because there are abortive respiratory efforts during the intrauterine period, it would be difficult to determine whether the flattening of the mucosa covering the vocal folds occurs as a result of these intrauterine motions or as the result of the actual crying motions of the newborn child. The ideal solution to this problem would be to obtain

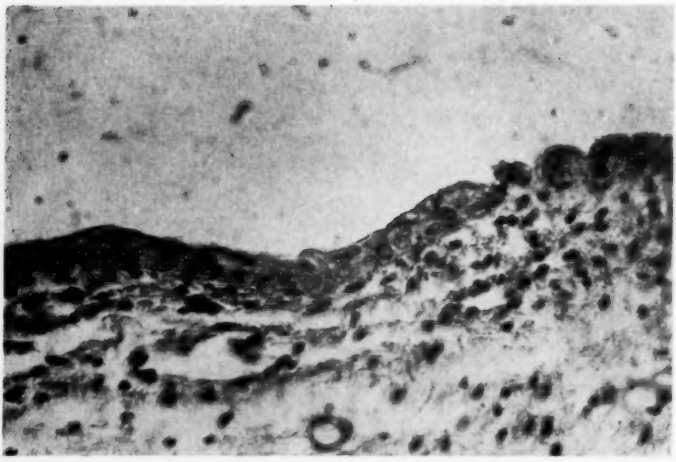

Fig. 2.—Coronal section (x450) through the true cord mucosa from the anterior one third. Although the mucosa is primarily composed of cuboidal cells, there is slight flattening in areas.

laryngeal sections from a fetus in which the larynx was well-formed and yet in which it could be determined that the child had never breathed. Recently a most unusual opportunity was presented to study the larynx from two specimens in which it could be ascertained for certain that respiration had not occurred. These were from two fetuses which were definitely alive until immediately before parturition. Both died shortly after birth because of impaired respiration. At postmortem examination it was found that both infants had complete pulmonary agenesis. Both of these cases will be reported in detail from the pathological standpoint in a later communication.

The developmental anomaly of complete pulmonary agenesis is in itself an extreme rarity and therefore this opportunity is unexcelled. To date in the world literature this defect has been reported on only five authenticated occasions. Roderer,[55] in 1754, observed a fetus with complete pulmonary agenesis in which the larynx ended blindly. The thorax contained only thymus and an incompletely developed heart. In place of the lungs there was a thick jelly-like, watery tissue without evidence of pulmonary arteries or bronchi. Schmit, in 1893, reported another case of complete absence of the lungs. There was only the heart in the thoracic cavity and no pleural

membrane. The larynx was well-developed. The trachea was not separated from the esophagus. Pulmonary veins were absent and the pulmonary artery was connected to the descending aorta by a large ductus botelli. Saito,[57] in 1902, found an instance of bilateral agenesis of the lungs in which there was only the heart in the thoracic cavity. The isthmus of the thyroid gland was absent. The trachea was separated from the esophagus and the larynx ended blindly at the level of the cricoid. In Mollison's[58] case of complete lung agenesis the right and left main bronchi ended in the bifurcation at the carina. Allen and Affelback,[59] in 1925, observed one fetus in which there was no other anomaly except for bilateral agenesis of the lungs. The trachea ended blindly at the level of the root of the heart with two one-millimeter pouches representing the main bronchi. In another reference cited by Ogamada, Lukin[60] reported two cases of entire absence of the lungs. However, this latter article is not available for study to confirm the pathological findings. Therefore, to this date there are five verifiable cases of complete pulmonary agenesis in the world literature and two cases which are reported but cannot be confirmed. Many others have reported cases with partial pulmonary maldevelopment. The literature pertaining to pulmonary agenesis, complete and partial, has been very well summarized by Valle,[61] Oyamada,[62] Boyden[34] and Smith and Bech.[63]

## METHOD OF STUDY

Both of the fetuses (A-162-56, 57-A-128) which were investigated were the result of full term, apparently normal pregnancies. In both cases they came to postmortem examination because death occurred immediately after birth. In both instances, the pulmonary findings explained the immediate cause of death, inability to respire. In both instances the fetuses were well developed and essentially normal appearing, physically. There were no other significant congenital anomalies noted in either instance. The pulmonary abnormalities were interesting and unexpected findings at the necropsy.

Gross examination of the oral cavities, tongues, pharynxes and hypopharynxes was normal in both instances. The larynxes were well-formed and anatomically normal. The false and true cords were well-developed. The laryngeal ventricles, epiglottises, aryepiglottic folds and paralaryngeal tissues were not abnormal. In both instances the trachea was well-developed, about 35 mm in length and ended in a blind pouch. There was no vestige of lung tissue in either case, although in case 57-A-128 there were small fibrous bands extending

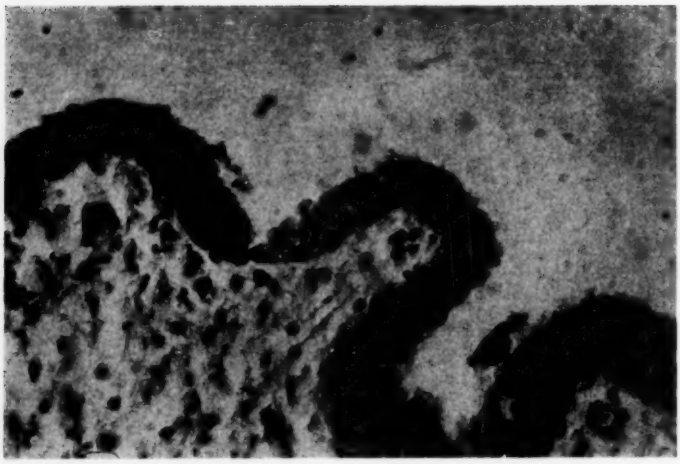

Fig. 3.—Coronal section (x450) showing the true cord mucosa in the area of the anterior commissure. The majority of the epithelial cells are of low cuboidal shape. A few show evidence of flattening.

from the tip of the trachea into the tissue of the thoracic cavity near the diaphragm.

Tissue removed from the fetal larynxes was mounted so that sections were cut in the long axis of the larynx. In this manner the mucosa could be traced from the aryepiglottic fold to the infraglottic area, across the false and true vocal cords. Multiple sections from the different portions of the larynx from anterior to posterior were made and examined. The mucosal pattern of the entire larynx was evaluated with special emphasis on the type of epithelium covering the true vocal cords.

The mucosa covering the false and true vocal cords in case 57-A-128 was found to be very well preserved so that the details of the histological architecture were readily apparent. The mucosa covering the false and true cords of specimen A-162-56 showed a moderate degree of autolysis in some portions, making identification of the exact cell type on the free edge less easy. However, enough of the cellular outlines were preserved so that it could be ascertained what type of epithelium was present.

In both instances the mucosa covering the false cords, the ventricles, the infraglottic portions of the vocal cords and the area superior to the false cords was composed of a stratified, columnar, ciliated epithelium. The mucosa covering the true vocal cords was found to be a flattened stratified epithelium, composed primarily of cuboidal cells on the free surface of the cords. Occasionally cilia were seen on cells located very near to the edge of the true vocal cords. There was no evidence of keratinization of the epithelium apparent in sections examined from various portions of the cords. There was no apparent difference in the character of the mucosal epithelium taken from different portions of the true cords.

The findings here would suggest, in view of the fact that these two fetuses could be proved conclusively not to have respired after birth, that any change seen in the mucosa covering the true vocal cords took place before respiration began. The vocal cord mucosal changes probably take place primarily after birth, with the respiratory, crying and coughing efforts of the child. The fact that there was found to be a flattening of the mucosa over the true cords, into a cuboidal rather than the tall columnar cell type found in other portions of the larynx and tracheobronchial tree, suggests that there is some degree of metaplasia of the epithelium, probably caused by the abortive respiratory and crying efforts of the fetus *in utero*. This most likely initiates the stretching of the mucosa covering the vocal cords which leads to an alteration in the cell types of the epithelium. Then after birth the process is completed, as the child traumatizes the cord mucosa, the columnar or cuboidal epithelium is replaced by stratified squamous epithelium. This epithelium gradually forms the typical keratinized epithelium which is more resistant to trauma and persists throughout the individual's life.

## COMMENT

In the search for causative factors to promote the treatment of disease, numerous items, many seemingly unimportant, must be considered and ruled out as etiological agents. Various new growths, malignant and nonmalignant, still defy the search for an exact cause. It is entirely possible that the elusive cause lies within the grasp of present day knowledge, if only the key were more readily apparent. Malignant neoplasms in the larynx comprise 2 per cent of all human malignant tumors. Although this is a small percentage of the total malignancies, it is a large enough number that attention must be focused upon any potential causative agent. In the present study, attention has been directed toward two factors which may play a

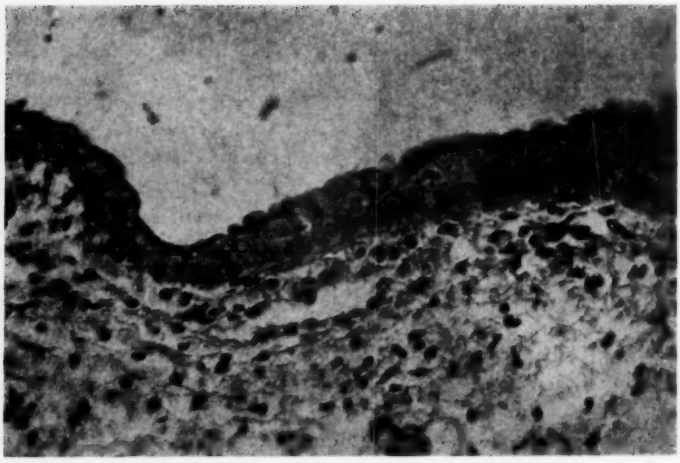

Fig. 4.—Coronal section (x450) through the true vocal cord from the posterior portion of the larynx. The epithelium varies from stratified cuboidal cell type to definitely flattened epithelium. There is no evidence of keratin formation. This type of flattening suggests metaplastic change in the superficial cells rather than primary squamous cell formation.

large role in the encouragement of new growths in the larynx. These are: 1) the physiological metaplasia which occurs in the mucosa covering the true vocal cords during the prenatal and postnatal periods, 2) the fact that while laryngeal neoplasms are relatively common in humans, they are rare in animals below man. This second factor suggests that something other than the physiological metaplasia which occurs in an animal's larynx is the most important in the production of neoplasms in the larynx.

In the past, the epithelium covering the vocal cords has usually been reported to be squamous. This is the situation in the adult and in the child after birth. It is not commonly known that the laryngeal mucosa is, in actuality, metaplastic. Examination of the mucosa covering the interior of the larynx in fetuses has been done by Hopp and others. This has shown that there is metaplasia of the mucosa covering the true vocal cords, from a columnar or cuboidal epithelium to a squamous epithelium. Examination of the laryngeal mucosa from two fetuses which had complete pulmonary agenesis but which were alive until birth has provided a valuable clue as to the nature of the

epithelium which covers the true vocal cords up until the actual time at which respiration commences.

The findings of this study support the contention of Hopp that there is physiological metaplasia of the mucosa covering the true vocal cords. Although his study suggested that the change in the mucosa takes place in the antenatal period, the findings here indicate that the metaplasia from columnar or cuboidal cell type probably does not occur until at or after birth, probably with the respiratory and crying efforts of the newborn child. The fact that there is metaplasia of the mucosa covering the true vocal cords is the important thing.

Investigation from the veterinary standpoint indicates that neoplasms of the larynx are a rarity in animals below man in the phylogenetic scale. Although neoplasms in this location have been reported, they are extremely unusual. The fact that physiological metaplasia of the true vocal cord epithelium occurs in lower animals as well as in man would suggest that the metaplasia per se is not a predisposing factor in the production of laryngeal new growths. So far, there has been no recorded experimental study done in an effort to stimulate the production of a laryngeal neoplasm in an animal below man. Therefore, it cannot be stated whether such a malignant new growth is possible in the laboratory.

It must be concluded that there is some factor in man, either phylogenetic, dietary, environmental, habit or due to voice use or abuse which differentiates him from lower animals in the ability to develop new growths. The possibility of experimental production of malignant new growths in lower animals using one of these avenues of approach offers promise for the discovery of the cause of laryngeal neoplasms in man. Investigation of this problem in the future is to be encouraged.

## CONCLUSIONS

1. Malignant tumors in the larynx of man are a relatively common neoplasm, comprising about two per cent of all human neoplasms. These malignancies have increased in frequency in the past fifty years.

2. In the recorded veterinary literature and in the large veterinary institutes today, primary neoplasms in the larynx of lower animals are a rarity.

3. Metaplasia of epithelium from one cell type to another is often a precursor of malignant change. Although the metaplasia may be

physiological, if this tissue undergoes frequent trauma or irritation, it may have malignant propensities greater than tissue which has not undergone metaplastic alteration.

4. Physiological metaplasia of the epithelium covering the true vocal cords occurs in the larynx either before birth or with the stretching and trauma to the cords associated with the respiratory motions or crying efforts.

5. The fact that neoplasms of the larynx are infrequent in lower animals suggests that the physiological metaplasia of the true vocal cord mucosa is not a primary factor in the production of laryngeal carcinoma.

6. In man, laryngeal malignancies are probably related to certain factors which do not appear in lower animals. These may include voice use and abuse, habit patterns including the use of tobacco, bidi, alcohol, betel nuts, occupational irritants and fumes, infections such as syphilis and tuberculosis.

7. Experimental production of cancer of the larynx in laboratory animals offers a possible solution to the question of etiology of this type of neoplasm.

14 Riverview Heights

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XLVI

# ELECTRONYSTAGMOGRAPHIC STUDIES OF VESTIBULAR FUNCTION:

## III. THE INFLUENCE OF VARIOUS ELECTRODE ARRANGEMENTS

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### PRELIMINARY INVESTIGATIONS

In our previous paper, we described a method for amplitude measurements of the fast component of vestibular nystagmus. This method is based on the electronystagmographic (ENG) recording of the corneoretinal potential changes which are produced by eye movements and which are registered with standard EEG equipment (Arnold, Giuliani and Stephens, Arnold and Miskolczy-Fodor).

Applying the method and experimental situation as described before, we attempted to improve the sensitivity of the ENG tracings obtained with the EEG apparatus (Grass Model IIID). In order to avoid mixed amplitude-velocity responses, we selected a very short time constant (EMG = 0.05 sec). Hence, we considered our electronystagmograms as pure velocity tracings of the nystagmic eye movements. This consideration is important for the further evaluation of our results.

### TECHNICAL PRECAUTIONS

The corneoretinal potential change, like that of all other D.C. biopotentials, is a change without a true threshold and without any

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quantal character. Yet, such potential changes must reach a certain quantity to become registrable. This is not a true threshold, because it depends only on the efficiency of selective amplification. Almost infinitesimal potential changes can be picked up, if the disturbing internal or external influences can be minimized. These disturbing influences can be divided into three main groups: 1) internal artifacts, 2) external artifacts, and 3) other bioelectric potentials.

1) *Internal artifacts*, such as noise and hum, are generated in the amplifying system.

2) The *external artifacts* consist mostly of disturbing electromagnetic radiations which are produced by the A.C. currents supplied for general household purposes. Therefore, efficient electric shielding is necessary to minimize these artifacts. The tested person must sit in a wire mesh cage and the peri-ocular electrodes are connected to the amplifier with shielded cables. While these artifacts present purely technical problems, it is more difficult to exclude other disturbing bio-electrical potentials arising elsewhere within the body of the tested person.

3) Several other types of bio-electric potentials are picked up together with the corneoretinal potential; these include brain waves, muscle potentials, cardiac potential changes, and others. These artifacts appear as an irregular, wavy instability of the tracing's base line. They increase with tension and body movements.

The corneoretinal potentials can be measured only if they produce pen-excursions with an amplitude which is significantly larger than that of the disturbing base line oscillations. Faint movements of the eyes may elicit potential changes which are so small that their spikes cannot be distinguished from the base line artifacts. No overall amplification may help in this case, because it amplifies without discrimination both the disturbing potentials and the potential changes under observation. On the other hand, the filters for muscle potentials, as installed in standard EEG equipment, begin to eliminate the frequencies above 40-50 cps.

### SUITABLE ELECTRODE ARRANGEMENTS

There is only one way to make electronystagmography more sensitive for the recording of corneoretinal potentials and this is the

selective amplification of the corneoretinal potential by means of an appropriate arrangement of the electrodes. The efficiency of this arrangement depends on three factors: 1) firm electrode attachment, 2) distance between the electrode and the eye, and 3) optimal electrode position.

1) An efficient electrode attachment requires firm and stable contact between electrodes and skin.

2) The nearer the electrode is placed to the source of the potential (corneal and retinal eye pole), the stronger is the recorded potential.[9-11] An electrode attachment within the orbital margin, or by means of a contact eye-glass, seems to be more effective than attachments outside the orbital margin, where a bony layer increases the resistance between the electrodes and the electrical eye-poles. The minimal possible distances for such an arrangement depend on the individual anatomical conditions; if the electrodes are attached too near to the eyelids, they irritate the patient and stimulate undesirable blinking reflexes. Contact eye-glasses, on the other hand, may alter the nystagmic movements.

3) The basic working principle of ENG is the amplification of the potential difference (and of the actual change in this difference) between two electrodes. In the course of eye movements one electrode picks up increasingly positive potentials, and the other increasingly negative potentials. The greater the difference between the recorded potentials, the stronger is the response. Again, the potential difference depends on the placement of the electrodes. It follows that the best position is near the electrically neutral equatorial parts of the eye bulb.[12]

## EXPERIMENTS WITH ELECTRODE ARRANGEMENTS

In order to obtain precise values of the relations between electrode arrangement and recorded eye response, we compared various types of electrode arrangements for the registration of horizontal eye movements (Figs. 1-3). Each comparison was made through the same channel and with the same amplification of the EEG apparatus.

1) The basis of these comparative experiments was the arrangement No. 1 which is suitable for the separate registration of the horizontal movements of each eye (Mahoney, Harlan and Bickford).

In other words, we selected this arrangement for a *standard reference* (Fig. 1).

2) Electrode arrangement No. $2^{14}$ (Fig. 2) produced spikes which were about 1.3 times smaller than those obtained with our reference arrangement No. 1.

3) Similar findings were made with the electrode arrangement No. $3^{3}$ (Fig. 3). It proved less effective than the reference arrangement with a ratio varying between 1.04 and 1.30.

For the registration of horizontal eye movements electrode arrangement No. 1 produced the clearest recording effects with regard to the response/artifact ratio. This arrangement seemed to be very appropriate, especially in cases of differences between the movements of both eyes, such as with disassociated nystagmus. However, in certain cases we were not satisfied with the efficiency of this arrangement. Sometimes we obtained for 2½ degrees of eye deviation spikes of very small amplitude (re artifacts). As a result of individual differences in skin resistance, skull form, etc., the 2½ degree spikes were, in such cases, hardly distinguishable from the base line oscillations.

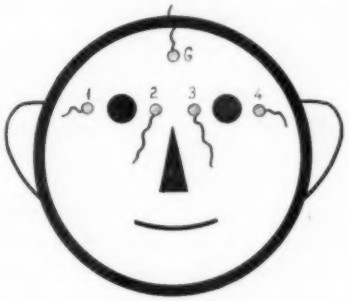


Figure 1
Electrode arrangement No. 1
G = ground electrode

Figure 2
Electrode arrangement No. 2
G = ground electrode

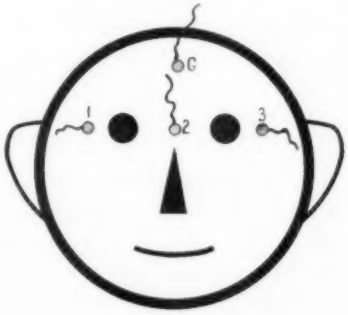


Figure 3
Electrode arrangement No. 3
G = ground electrode

This deficiency limited the practical value of that arrangement. If small nystagmus amplitudes (below 3 degrees) cannot always be clearly recorded and measured, one obtains an end point in the ENG record before the true termination of the vestibular reaction, suggesting a shorter duration. Since ENG aims at the full registration of the total nystagmus duration, it is important to measure as many of the decaying nystagmus beats as is technically possible.

4) As a rule, both eyes perform associated movements during nystagmus. It is therefore sufficient to record the movements of both eyes together. Such an arrangement offers many advantages, including the easier and more rapid evaluation of the ENG records.

According to theory, the potential differences of both eyes should appear summarized between the bitemporal electrodes of arrangement No. 1[13] (Fig. 1). This electrode arrangement is used also by Mackensen and Henriksson. As expected, this electrode arrangement was more efficient with regard to the response/artifact ratio than when arrangement No. 1 was used for the separate recording of each eye.

In our experiments the bitemporal lead produced a recording effect which was about 1.73 times greater (ranging between 1.23 and 2.56) than our reference arrangement No. 1 (Fig. 1), or the electrode arrangement No. 3 (Figs. 3-5). Furthermore, the spikes of the bitemporal tracing were almost four times *higher* than those obtained with arrangement No. 2 (Fig. 2).

All these results were computed by averaging the responses to two types of induced eye movements, namely of five and ten degree amplitude, which are in the range of average nystagmus deviation. Our method to induce measurable eye movements and our principle of evaluation was described in a previous paper.[2]

## ADVANTAGES OF BITEMPORAL ELECTRODES

As discussed above, the use of bitemporal electrodes has the advantage of a stronger recording effect. Consequently, the response of all eye movements is enhanced to such an extent that they are easily distinguished from the base line artifacts. In this manner, we rarely encountered difficulties in recording eye movements of less than two and one-half degrees. As a result of the increased response/artifact ratio we could reduce the over-all amplification and consequently all artifacts were also reduced.

TABLE I

VARIABILITY OF SINGLE SPIKE VALUES (AMPLITUDE AND TERRITORY) IN ENG TRACINGS ACCORDING TO DIFFERENT INDUCED EYE MOVEMENTS AND DIFFERENT ELECTRODE ARRANGEMENTS

| ELECTRODE ARRANGEMENTS | | DEGREE OF INDUCED EYE MOVEMENTS 5° | | 7.5° | | 10° | | 15° | | 20° | | 32.5° | | Average | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY | AMPLITUDE | TERRITORY |
| Bitemporal lead | St.d. | 0.32 | 0.58 | 0.63 | 0.47 | 0.58 | 0.39 | 0.66 | 1.26 | 0.61 | 1.86 | 0.97 | 1.4 | 0.66 | 1.14 |
| | St.e.m. | 0.06 | 0.13 | 0.14 | 0.11 | 0.12 | 0.15 | 0.15 | 0.28 | 0.14 | 0.50 | 0.22 | 0.35 | 0.21 | 0.26 |
| Binocular leads (Fig. 1) | St.d. | 0.66 | 0.83 | 0.69 | 0.81 | 0.71 | 0.99 | 0.80 | 1.77 | 0.97 | 2.1 | 0.88 | 3.4 | 0.79 | 1.35 |
| | St.e.m. | 0.15 | 0.19 | 0.15 | 0.19 | 0.16 | 0.22 | 0.24 | 0.39 | 0.22 | 0.47 | 0.19 | 1.3 | 0.24 | 0.22 |
| No. 3 (Fig. 3) | St.d. | 0.64 | 0.66 | 1.05 | 1.17 | 0.97 | 1.1 | 1.32 | 1.5 | 0.87 | 1.81 | 1.07 | 1.8 | 1.05 | 1.40 |
| | St.e.m. | 0.15 | 0.15 | 0.24 | 0.25 | 0.21 | 0.25 | 0.39 | 0.34 | 0.19 | 0.40 | 0.20 | 0.35 | 0.23 | 0.15 |
| No. 2 (Fig. 2) | St.d. | 1.8 | 2.7 | | | 1.55 | 1.52 | | | | | | | 1.68 | 2.19 |
| | St.e.m. | 0.39 | 0.46 | | | 0.35 | 0.35 | | | | | | | 0.26 | 0.29 |

St.d. = standard deviation

St.e.m. = standard error of the mean

The results represent ± values in degree of eye movement computed from mm resp. $mm^2$ values of the actual measurements.

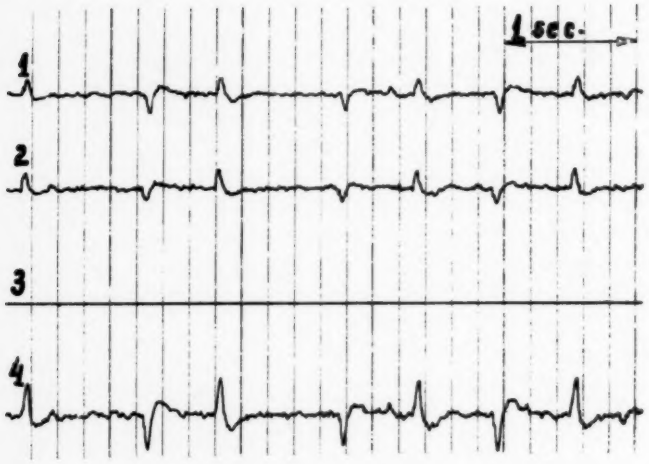


Fig. 4.—Tracings obtained from the bitemporal and the monocular electrodes of arrangement No. 1 (see Fig. 1: bitemporal between 1 and 4, monocular between 1 and 2, resp. 3 and 4). Induced eye movements of 5°. Upward spikes indicate horizontal movements to the right, and downward spikes those to the left side.

Tracing 1 refers to the right eye, 2 to the left eye, and 4 to the bitemporal leads. All tracings were obtained with equal amplification in different channels. The computations were made from tracings obtained not only with equal amplification, but through the same channel. Note the increased response from the bitemporal leads.

The practical application of our experimental results did not confirm any stable ratios in the relations between the responses obtained by the different electrode arrangements as had been suggested by Miles. Variations over fairly large ranges were observed among different persons (see also Figs. 4 and 5). These deviations were less marked for different eye movements of the same person. This fact can be explained by differences of tissues resistance. Variability in the anatomical configuration may also introduce additional variables. When comparing the efficiency of various electrode arrangements, one must bear in mind that such comparisons are limited by certain individual variations which can hardly be controlled.

Although the bitemporal electrode effect was not always the precise sum of the two monocular effects, we became convinced that the use of the bitemporal electrode arrangement was significantly superior

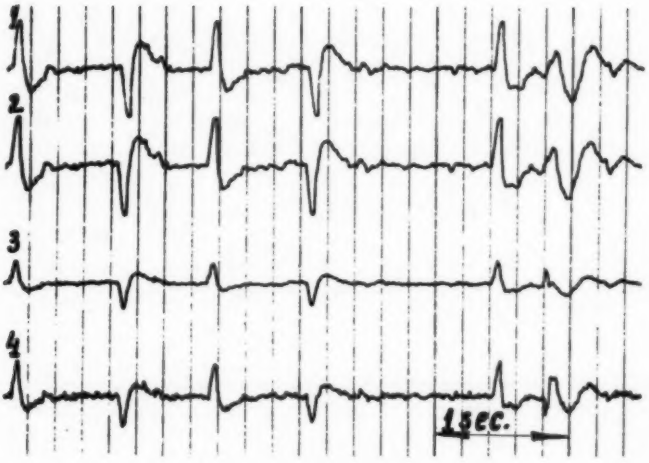


Fig. 5.—Tracings obtained from the bitemporal and monocular electrodes of arrangement No. 3 (see Fig. 3: bitemporal between 1 and 3, monocular between 1 and 2, resp. 2 and 3). Induced eye movements of 10°. Upward spikes indicate horizontal movements to the right, and downward spikes those to the left side.

Tracings 1 and 2 show the same bitemporal pattern through two separate channels, tracing 3 refers to the right, and 4 to the left eye. All tracings were obtained with equal amplification in different channels. The computations were made from tracings obtained not only with equal amplification, but through the same channel. Note the increased response through the bitemporal leads.

to all other leads. On the basis of our results we prefer the use of this type of electrode arrangement. It is obvious that the sensitivity of ENG increases with the smallest eye movements that can still be differentiated from other bio-electric features. In other words: the smaller the recognizable eye movements are, the greater is the sensitivity of the method. This fact is practically important. Vestibular reactions terminate with a gradual decay of the nystagmus intensity (frequency, amplitude, etc.). The longer one can follow the recorded nystagmus beats, the greater will be the value of the recorded total nystagmus duration.

Another advantage of the bitemporal electrode arrangement is the fact that it does not register disturbing convergent or divergent

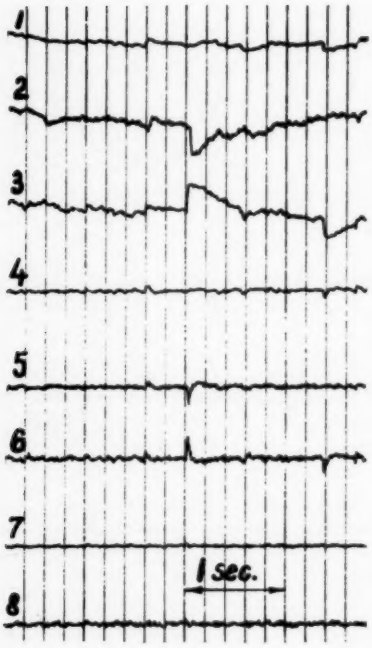


Fig. 6.—Convergent eye movement under the Frenzel goggles. Tracing 1 was obtained from the bitemporal leads, 2 from the right eye, and 3 from the left eye with electrode arrangement No. 3; long time constant (0.3 sec). Tracing 4, 5, and 6 were obtained from the same leads, but with short time constant (0.05 sec). Tracings 7 and 8 were obtained through vertical leads.

eye movements. These appear occasionally under the Frenzel goggles which minimize ocular fixation, as shown in Figure 6.

Examined on five persons, the use of bitemporal electrodes revealed the same relationship among spike amplitude, spike territory, and angle deviation of induced "voluntary" eye movements, as was found with electrode arrangement No. 1. This general relationship was described in our previous paper.[2] However, the tracings obtained with bitemporal leads showed less standard deviation between the individual spikes of the nystagmogram (Table I). This indicates again the greater stability and reliability of the bitemporal leads in comparison to other electrode arrangements.

PRACTICAL APPLICATION

After having worked with the bitemporal electrode arrangement for some time, we became increasingly impressed with its advantages. This led to the development of the following procedure for our routine registration of ENG. As before, we use the EEG apparatus (Grass Model IIID) for the registration of the corneoretinal potentials. Channels and electrodes are arranged in the following manner (Figs. 7 and 8).

Three channels with the EKG time constant (0.3 sec) serve for recording from the bitemporal leads, as well as from 2) the right and 3) the left temporonasal leads, all for the horizontal eye movements. Three further channels are used for the *same* electrode arrangement, but with the EMG time constant (0.05 sec). They produce the desired velocity tracing of our recording procedure. The last two channels, also with EMG time constant, record the vertical movements of each eye.

Fig. 7.—Electrode arrangement used for routine investigations. The bitemporal record is obtained from electrodes 1 and 3; the right eye is recorded from leads 1 and 2, and the left eye between 2 and 3; the vertical electrodes are 4 and 5, resp. 6 and 7. G = ground electrode.

The temporonasal leads for each eye are placed according to arrangement No. 3. In our experience, the placement of electrodes too near to the eye lids and the inner canthus (as in No. 1) irritates a sensitive patient and increases the blink reflex. By avoiding this inconvenience we gain more than we are losing with the slightly decreased sensitivity of this electrode arrangement as compared to arrangement No. 1. However, when it appears that the bitemporal electrodes will not be suitable, such as in a case of dissociated nystagmus, we would prefer arrangement No. 1.

In all eight channels the nystagmus is registered during the course of the entire vestibular reaction (Fig. 8). However, we use only the single tracing of the bitemporal EMG registration for the subsequent evaluation of our velocity records. All other channels

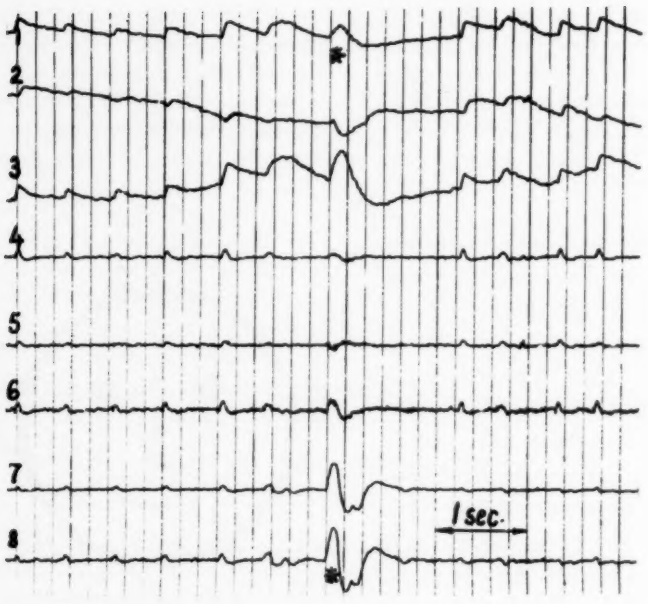


Fig. 8.—Tracing obtained with electrode arrangement shown in Fig. 7. Tracing 1 is the bitemporal record, 2 records the right eye, and 3 the left eye, all with long time constant (0.3 sec). Tracings 4, 5, and 6 refer to the same leads, but with short time constant (0.05 sec). Tracings 7 and 8 record the vertical eye movements. In these two curves upward spikes indicate movements directed upwards, and vice versa. Horizontal movements are defined as in Figure 4. The tracing shows a horizontal nystagmus with the fast component to the right, and a blink reflex at point (x).

serve for the recognition of disturbing or dissociated eye movements: convergent-divergent movements (Fig. 6), blinking (Fig. 8), differences in the movements of both eyes, etc. The simultaneous registration with the longer EKG time constant is sometimes helpful for the differentiation of minute nystagmic spikes in the velocity tracing which is obtained with EMG time constant.

The vertical leads facilitate the recognition of various involuntary vertical eye movements or blinking. All such accidental eye movements are accompanied by some deviations in the tracings from the vertical electrodes, whereas horizontal (or horizontal-rotatory) nystagmus shows no effects in the vertical leads. In this connection

it must be mentioned that the rotatory component of some vestibular nystagmus forms cannot, at the present time, be registered by means of corneoretinal potential changes.

The separately registered tracings of each eye are not evaluated any further, except in cases of dissociated or asymmetrical eye movements.

SUMMARY

Several technical factors were discussed which may influence the response/artifact ratio of electronystagmographic recordings. A suitably selected and properly applied electrode arrangement determines to a large extent the success of ENG. The efficiency of several electrode arrangements was investigated and compared.

According to the results of this comparison, the bitemporal electrode arrangement produced the most sensitive recordings with the clearest responses. Further advantages and some disadvantages of the bitemporal leads were discussed in detail.

Based on these experiences, the authors established a routine procedure for electronystagmographic recordings which can now be recommended for clinical investigations.

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# The Scientific Papers of the American Otological Society

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## XLVII

## AN INTERPRETATION OF THE MECHANICAL DETECTOR ACTION OF THE COCHLEA

HALLOWELL DAVIS

WITH

DONALD H. ELDREDGE
(by invitation)

ST. LOUIS, MO.

Last year I reviewed with this Society a theory of the mechano-electrical action of the cochlea that undertook to account for the excitation of nerve impulses as a result of the bending of the hairs of the hair cells.[4] In that paper I described the resting DC potentials of the endolymphatic space and the interior of the hair cells and also the two electrical responses, namely, the cochlear microphonic and the summating potential. I reviewed briefly the experiments which had led us to associate the cochlear microphonic response with the external hair cells specifically and the summating potential with the internal hair cells.

According to my theory both the alternating-current microphonic of the external hair cells and the direct-current summating potential of the internal hair cells serve as intermediate steps between the mechanical bending of the hairs and the initiation of nerve impulses in the nerve endings at the opposite ends of the hair cells. The summating potential and the cochlear microphonic seem to have

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fundamentally the same origin and function. One of the problems that I propose to discuss today is how a steady one-way (DC) bending of the hairs of the internal hair cells can reasonably occur while the hairs of the external hair cells are at the same time being bent back and forth by every individual cycles of sound wave. I shall propose a model for the mechanical "detector" which I told you last year we must postulate in the acoustic workings of the cochlear partition.

The cochlear microphonic has a curious property that I mentioned briefly but did not explain. This is its input-output relation to the acoustic stimulus. In the basal turn of the guinea pig cochlea and for frequencies above about 4000 cps the voltage of the cochlear microphonic increases at first in direct proportion to the intensity of the sound. Above about 80 db the output rises less and less rapidly and it goes through a maximum between 100 and 110 db. At still higher intensities the cochlear microphonic becomes progressively smaller and smaller. This effect, a maximum in an input-output curve, is unusual in itself but it is even more remarkable that the cochlear microphonic remains sinusoidal or very nearly so even when it has reached its maximum or gone on to the supramaximal reduction in amplitude. It has been difficult to conceive in terms of a mechanical model how this might occur.

## THE DETECTOR ACTION OF THE COCHLEA

Let us accept the propositions, 1) that the cochlear microphonic is an alternating-current output of the external hair cells, 2) that it is generated at the cuticular layer, probably just at the base of the hairs, and 3) that it depends on a bending (or shearing) of these hairs. The bending or shearing of the hairs occurs because one end of each hair is fixed in a hair cell that forms part of the reticular lamina while the other end is embedded in the tectorial membrane. The tectorial membrane, you will recall, is fairly stiff and is composed of fibers embedded in a viscous gel. The outer and the inner edges of the tectorial membrane are attached to the cells of Hensen and the inner supporting cells respectively of the organ of Corti, but its major point of attachment, around which the tectorial membrane swings as on a hinge, is the lip of the limbus. The tectorial membrane pivots at this point while the basilar membrane and one edge of the organ of Corti pivot at the point where the flexible basilar

membrane attaches to the rigid bony lamina spiralis. As the cochlear partition bulges up and down, the tectorial membrane and the reticular lamina must shear past one another because their hinge points are at different levels.

As the hairs are bent back and forth the cochlear microphonic goes through a single cycle of electrical change. The cochlear microphonic goes relatively positive when the hairs are bent in one direction and relatively negative when they are bent in the opposite direction. This behavior, incidentally, is different from that found in the lateral line organs of certain fish in which the outer surface of the hair cells becomes more negative whichever the direction in which the hairs are bent.[8] In this organ there are therefore *two* electrical cycles for each full mechanical cycle. In the cochlea, however, the mechanism that relates the generation of the alternating electrical potential to the bending of the hairs is polarized so that there is only one electrical cycle for each mechanical cycle. It is equally important that, as Békésy has shown experimentally,[1] the direction of movement that is effective in the region of the *external* hair cells is a *radial* movement approximately parallel with the fibers of the tectorial membrane. Furthermore, he has shown that if the tectorial membrane is vibrated in a direction at right angles to the fibers of the tectorial membrane no cochlear microphonic is generated at the outer edge of the organ of Corti. Near the limbus, however, where the *internal* hair cells are located, a *longitudinal* movement of the tectorial membrane toward the helicotrema produces a negative electrical potential. This movement is approximately at right angles to the fibers of the tectorial membrane.

Our problem is to imagine how a steady one-way sliding of the tectorial membrane toward the helicotrema might result from the vibration of the cochlear partition. Such a one-way movement would account for the generation of the summating potential by the internal hair cells.

Remember that the over-all pattern of movement of the cochlear partition is not a synchronous bulging up and down of the whole length of the structure but a traveling wave. The wider, heavier, more flexible, apical portion of the partition lags behind the narrower, stiffer portion by a full cycle or more. Békésy[2] has explained in some detail how this pattern of movement is a necessary result of the

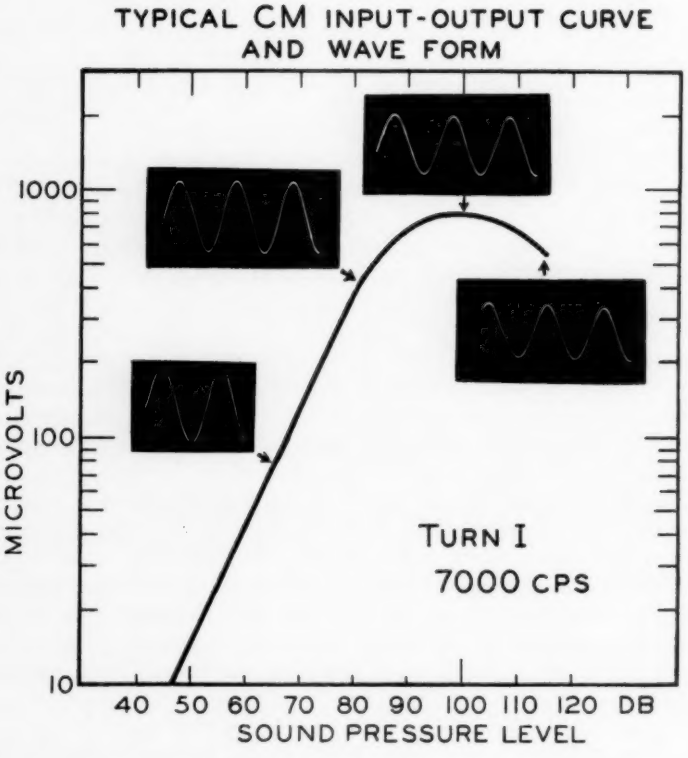


Fig. 1.—A typical input-output curve for the cochlear microphonic recorded from the first turn of the guinea pig's cochlea in response to frequencies above 4000 cps is linear up to about 80 db SPL and goes through a maximum at about 100 db SPL. The exact intensity values vary somewhat with the frequency. The oscillograms show the sinusoidal wave form recorded at the points indicated by the arrows. The amplification was adjusted to give oscillograms of approximately the same size. All of the responses are almost perfectly sinusoidal.

principles of resonant vibration as they apply to a continuous structure that has a gradient of stiffness. (The cochlear partition is such a structure.) The maximum amplitude of movement occurs in the region where the natural frequency of vibration corresponds to the frequency of the driving force, just as it would in a series of independent elements. The cochlear partition is a continuous structure, however, and each element is connected or "coupled" elastically to its neighbors on either side.

In a series of graded but independent vibrators the elements at the point of resonance move in step ("in phase") with the driving force. Those on one side that have higher natural frequencies tend to move too fast and to "lead" the driving force in phase. Those on the other side lag behind, and there is a difference in phase of as much as half a cycle between the elements on opposite sides of the one that is just matched to the driving frequency. In the region of resonance not only the amplitude of movement is greatest, but also the differences in phase. Therefore it is here that the *average instantaneous separation* between neighboring elements tends to be greatest.

Now in our actual continuous cochlear partition the elements are coupled elastically to one another and cannot separate more than a very little as they vibrate. It is the longitudinal continuity or coupling that prevents them from separating as they would otherwise do. The apical regions are always tending to lag behind the more basal stiffer regions, enough to restrain the basal region in its movement and make it lag behind the driving force in phase instead of leading it. *The cochlear partition is thus subjected to a steady longitudinal stretching force between its neighboring elements.* And this force, acting on the longitudinal couplings, will tend to be greatest in the region of resonance where both the amplitude and the phase differences tend to be greatest.

Both the basilar membrane with the organ of Corti on it and the tectorial membrane are parts of the vibrating cochlear partition and therefore the longitudinal stretching force appears in each of them. *We need only to assume that the tectorial membrane actually stretches a little more than the basilar membrane and the organ of Corti.* This is a reasonable assumption because the tectorial membrane has only radial but no longitudinal fibers. If the tectorial membrane stretches more it must slide a little relative to the basilar membrane.

It is not quite so obvious why the tectorial membrane should slide toward the apex rather than in both directions away from the region of maximum amplitude. The direction is related somehow to the direction of travel of the traveling wave. Perhaps it can best be derived intuitively from Békésy's[2] description of how the stiffer (basal) portion of the partition that leads in phase tends to "drive" the more apical portions that tend to lag.

Our model meets another requirement of experimental observation. The DC summating potential is localized along the cochlear partition to the region of phase differences and longitudinal bending of the traveling wave pattern.[3,5] The summating potential is actually much better localized than the cochlear microphonic. Thus the inner hair cells have at least the potentiality of providing better place discrimination of frequency than can the external hair cells. The summating potential may not appear at such low sound intensities as the cochlear microphonic, but it is probably a better frequency-analyzer.

In general terms, we believe that the inner hair cells are sensitive to a longitudinal stretching force that necessarily appears in the continuously graded structure of the cochlear partition and that is part of the same mechanism that determines the traveling wave pattern. The summating potential does not depend on second-order consequences of the traveling-wave pattern, such as the formation of eddies in the surrounding fluid which we invoked in 1957.[3] If we understand the mechanism that transforms vibratory motion into a one-way displacement of the tectorial membrane we may find that the generation of eddies in the fluid under conditions of very high amplitude follows as a simple corollary.

## LIMITATION OF THE COCHLEAR MICROPHONIC

The longitudinal slippage of the tectorial membrane that is a central feature of our model gives a probable explanation for the limitation of the voltage of the cochlear microphonic without distortion of wave form. Two possible mechanisms for this limitation have occurred to us and we are not yet able to decide between them on experimental evidence. Furthermore the two mechanisms are not mutually exclusive.

The first possibility is that when and where the tectorial membrane slips along the organ of Corti it stretches and pulls taut its

attachments to the organ of Corti along the outer border of the cells of Hensen. This tightening presumably limits the extent of the slippage, and the summating potential therefore grows more and more slowly with increasing intensity. We know that at first the growth is linear, but above 80 or 90 db it follows more nearly a square root or cube root law.[5,6] The mechanical coupling of tectorial membrane to organ of Corti presumably becomes closer and presumably there is therefore less relative movement *radially* between them than there otherwise would be. We suggest that this restraint is a possible reason for the departure from linearity in the input-output curves of both the summating potential and the cochlear microphonic.

Notice that our model preserves the sinusoidal wave form of the cochlear microphonic. The mechanical properties of the tectorial membrane-organ of Corti system are changed as a whole by the DC movement of the tectorial membrane. This is quite different from a vibrating mass reaching a non-linear limit at the peak of each cycle of displacement, which is the usual basis of a non-linear electroacoustic input-output curve. In such a case the individual waves become flat-topped or peak-limited. (Actually peak clipping does also appear in the cochlear microphonic mechanism, but only for lower frequencies. We shall consider it and its interaction with the undistorted limitation in another paper, now in preparation.)

Furthermore our model can explain not only the bending of the CM output curve but also the very similar remote effect of one tone in depressing the CM output of a different frequency. This effect was first described and fully investigated by Wever, Dray and Lawrence in 1940[9,10] but has received very little attention since that time. The "interference phenomenon" occurs only with rather high sound levels, above the limit of linearity for CM and SP, when the longitudinal stretching should be great enough to affect regions somewhat removed from the region of maximum phase differences and amplitude of vibration.

The second mechanism that may account wholly or in part for the reduced output of CM at very high intensities is a bending sideways, at right angles to their effective direction of movement, of the hairs of the external hair cells. In this position a given radial displacement of the outer end of the hair by the tectorial membrane may produce less movement at the base *in the proper direction* than it does

when the hair is upright, perpendicular to the reticular lamina. The sideways bending is assumed, of course, to be produced by the longitudinal slippage of the tectorial membrane. It is difficult to test or even to assess this suggestion until we know more about the details of the mechanism at the base of the hair cells by which mechanical movement in a particular direction controls the flow of electric current. Some very recent observations lead us to favor this second possibility, namely, that because of the longitudinal slippage a given amount of radial bending of the hairs produces less cochlear microphonic. The first possibility was that a given amplitude of displacement of the cochlear partition as a whole produces less radial bending of the hairs because the tectorial membrane becomes more closely coupled to the organ of Corti.

Both mechanisms are, of course, quite distinct from non-linear limitation of movement of the cochlear partition as a whole. This would produce peak limiting. Such peak limiting may occur, but we do not believe that the movements or the "tuning" of the partition as a whole are affected in any important way by the tightening of the attachments of tectorial membrane to the organ of Corti that we have assumed in our model.

## THE NON-NEURAL NATURE OF THE SUMMATING POTENTIAL

As a final comment we point out that our present interpretation of the summating potential is entirely different from our original interpretation when, with Fernández and McAuliffe, one of us first reported this direct-current response in 1950.[7] At that time we were searching for a local non-propagated response of the nerve endings that would have no refractory period and could therefore summate (in time) the stimulating effects of several high-frequency sound waves. We believed that we had discovered this neural response and therefore called it the "summating" potential. It took us several years to realize that the "summation" is actually a mechanical detector action and not a bioelectric reaction in the nerve endings. Fortunately, however, our name for it is still appropriate, for by transforming some of the alternating vibratory energy into a direct-current output the mechanical detector system does indeed summate the effects of several successive sound waves. Incidentally, we still think that there must be a process of temporal summation at the nerve

endings. It will be harder to find than we thought because it will be overlaid and obscured by our present "summating potential."

SUMMARY

A theory of mechanical action in the cochlear partition is proposed which accounts for the DC "summating potential" response of the inner hair cells and for the shape of the input-output curve of the cochlear microphonic at high frequencies. The latter goes through a maximum at about 107 db SPL (basal turn of guinea pig cochlea, 7000 cps tone bursts) without obvious distortion of wave form.

The major points in the theory are: 1) A longitudinal stretching force appears in the cochlear partition because neighboring elements of different natural periods are elastically coupled to one another. It is this coupling that constrains the partition to a traveling wave pattern of vibration. 2) The tectorial membrane is assumed to stretch more than the basilar membrane and therefore to slip slightly along the organ of Corti toward the apex. 3) The hairs of the inner hair cells are thus bent steadily toward the apex. This bending produces the DC summating potential. 4) The tectorial membrane becomes coupled more and more closely to the organ of Corti. Radial relative movement between them becomes progressively more restrained as intensity increases. This would account for the shape of the input-output curve of the AC cochlear microphonic, generated by the external hair cells. The interference phenomenon of Wever, Bray and Lawrence can be explained on the same basis. An alternative explanation of these effects on the cochlear microphonic invokes the interaction in the hair cells of a longitudinal bending with the familiar transverse bending of the individual hairs.

818 SOUTH KINGSHIGHWAY

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XLVIII

# SAMPLING AUDITORY RESPONSES AT THE CORTICAL LEVEL

## A ROUTINE FOR EER-AUDIOMETRIC TESTING

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AND

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Although standardization of Electroencephalic Response Audiometry (EER-Audio) is recent,[4,5,14] the use of the EEG as a key to internal flow of sensory information is at least a decade old. In the late 1940's, when the electroencephalogram was first used in the detection of auditory reception,[6,11] it was recognized as an ingenious experimental idea, with interesting theoretical implications, but was not utilizable in that form for more than gross diagnostic purposes.

The use of the EEG with the quantitatively measured sensory input of a standard audiometer was first reported by Giddoll a few years later.[8] But this valuable pebble sank without so much as a ripple. Recently in experimental and clinical laboratories the EEG response to sound are again being investigated. Geisler, Frishkopf and Rosenblith[7] are interested in these responses in regards to the communication system in man. Abe,[1] Suzuki[13] and Withrow[14] are interested in developing the clinical EER-Audio method. Abe and Suzuki have used the photographic superimposition of traces as originally sug-

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gested by Dawson.[3] Withrow and Goldstein have described a scoring system for the electroencephalic responses (EER) to sound and developed the three way relationship between the EER-Audio profile and the data given by "conditioning"—the EDR—and standard audiometric thresholds, but the number of such studies is not large. Most of those who hailed the preceptiveness of the first experimenters have unfortunately been content to let it go at that. Certainly, it is astonishing that the method has not been more widely incorporated into clinical diagnostic procedures.

As a diagnostic tool, in communication disorders, this process fills a true gap in clinical analysis. At present the EER-Audio method represents the single direct access to a part of the communication channel that bridges the sensory input and the motor output. This fact is acknowledged by clinicians, who have nevertheless failed to take the further step of putting the EER-Audio into their diagnostic work-ups. The objection of expense is a real one. In addition to the cost of the instrument itself the EEG requires space, and if it is used for audiometric measurement it makes special acoustical requirements of the space it occupies. But such factors do not account for the available and yet unused EEG facilities in many hospitals and clinics.

Cost excepted, the basic stumbling blocks in using the EER-Audio method are probably two. The first is the supposed need for expertness of the reader who is looking for the auditory response. The second barrier to general use of the test is the as-yet-unanswered question of the dependability of information provided by the EEG in this area. This paper proposes to provide at least partial answers to both of these problems.

In discussing the necessary qualifications for an EER-Audio reader, it is important at the outset to separate the task of evaluating the EEG pattern per se, for its clinical meaning, from the task of detecting an electroencephalic response (EER) to sound. Clinical interpretation is the province of the certified EEGer. It requires of him extensive clinical experience and detailed knowledge of the functioning of the central nervous system. He must be completely familiar with the forms of the separate and combined electrical patterns expressed on the EEG record, and with the probable relation of each EEG record to certain kinds of nervous system activity. In

contrast, the reading of an EER-Audio record is not dependent on certification or on the specialized knowledge which certification implies, but requires merely perceptiveness, diligence, and experience with the test. This paper aims to provide a procedure for administering the EER-Audio test, and to describe objective indices for the electroencephalic responses to sound which are not dependent upon the investigator's previous background in clinical EEG. By following the process (to be elaborated below), even a totally untrained person can become proficient in interpreting the EER-Audio, and overcome the first of the two obstacles to clinical use of the test.

The second question, that of the dependability of EEG studies of hearing, is more difficult to answer. The question cannot be asked or answered within the framework of traditional audiometry, since the EER method has a different perspective toward the whole hearing process than that of the conventional audiometric analysis. Obviously, the EER-Audio cannot be "validated" by simple comparison with the results of standard audiometry. If we choose 'agreement with a conventional audiogram' as our criterion for adequacy, there would be no reason for the innovation of a new method. Audiometry is a less expensive, quicker, and better-established procedure than the EER method, and would therefore be the preferable test, if the functions of the two methods were the same. Actually, these two tests tap entirely different points in the auditory process (Fig. 1).

This is not to say that such comparisons are not valuable and useful. In building up a clinical profile, the total picture is greatly enriched by compounding the information taken from Standard Audiometry, EER-Audio, EDR-Audio, the patient's history, and (at best) independent data from an entire multi-disciplinary team. A comparison of large numbers of parallel findings, by various kinds of audiometric test, is necessary if we would understand more fully the differences between all of these measures, and the relationships between the physiologic functions which produce the various test results.

But to compare any of these distinctly different measures, for the purpose of validating any one of them by agreement with the others is defeating the purposes of multiple testing. The act of hearing is a complex sequence of reactions, involving a number of structures and processes for its proper function (Fig. 1). The use of a

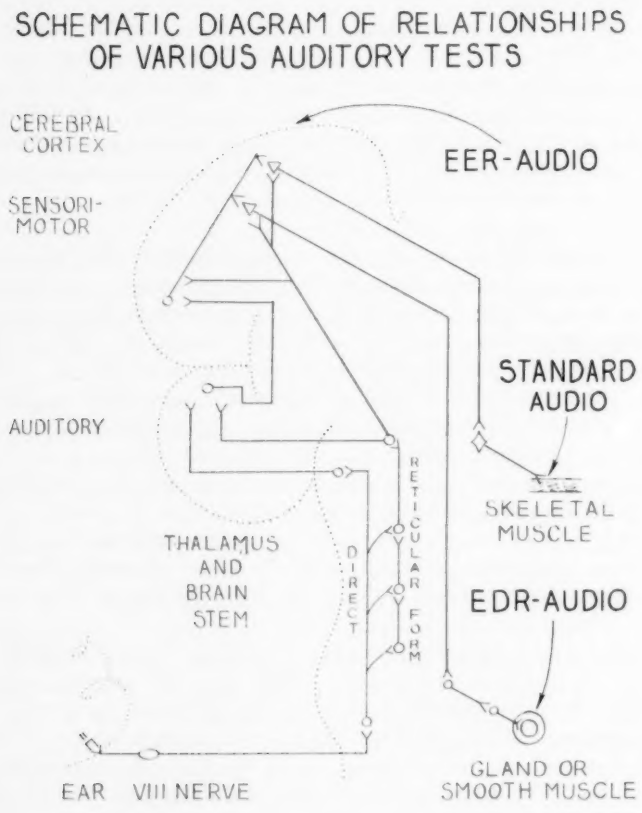


Fig. 1.—Schematic diagram of the auditory channel. Shows direct sensory path to the temporal lobe, and indirect path through reticular formation, to entire cortex. Where these paths join in the sensory-motor cortex, neurones are suggested for voluntary motor and visceral motor action.

Labelled on the right are the three places along the auditory channel at which three audiometric tests record their raw data.

variety of testing procedures recognizes this fact by sampling the response sequence at different "levels." The EER-Audio method, for example, probably samples the activity of a sensory limb, at the level at which some collateral aspect of auditory information is presented to the sensory-motor cortex. In contrast, standard audiometry measures a much later step in the process: the response, as a somatic pattern of behavior. Here (in the audiogram), the reaction tested is that of one of the final motor output points. Sensory presentation, perception, and pertinent conscious and unconscious psychic processes have all contributed to the producing of a particular behavior (i.e., raising a finger or pressing a button, to indicate having heard). It seems entirely likely that data taken at either of these two points (EER-Audio/standard audiometry) would differ, not only from each other, but also from EDR (PGSR) audiometry. The EDR samples the process still a different point in the total act of audition, because the "conditioning" which underlies the transfer of the sweating response from the shock to the originally neutral tone stimulus appears to take place at yet another level in the central nervous system.[12]

Differences in the auditory profiles taken at these quite distinct way-stations, far from casting doubt on any of the separate tests involved, may well be the best key to diagnostic distinctions between patients. For it follows that interference with the auditory message at the level of, e.g., sensory cortical presentation (EER-Audio), might have a very different significance to both therapist and patient than interference with the same auditory message at the motor output site (standard audiometry). It may well be that we can only hope to describe different auditory problems by means of reliably established differences in the information obtained by testing at the several physiologic levels. And if this is true, it should be our goal to determine both the dependability of each testing procedure, on the basis of its own findings, and its relationship to other testing procedures. Such comparisons may cast new theoretical light on familiar clinical categories of communicative disorders.

If we cannot validate the results of the EER-Audio by comparison with standard audiometry, or with any other audiometric test, how can we assess our results? The alternative to clinical cross-validation of a test is to create, for the test we wish to validate, a procedure for verifying the measurement by direct comparison with the processes it is alleged to detect. If we are able to judge correctly,

from the cortical activity alone, when an auditory stimulus is presented, we may have some confidence that we are looking at auditory responses. We can then set a level of confidence (in terms of the chance probability of any given number of correct "guesses") for accepting our results as valid.

In the present case, a process can be created by which the reader of the EER-Audio record assigns fixed numerical values to his judgements about the presence or absence of responses. These numerical "scores" can then be used to distinguish between periods of auditory stimulation and identically marked periods of no stimulation. By setting a 95 per cent confidence level and computing an empirical error-factor, we are able to establish a numerical value which must be reached or exceeded for a judgement to be considered valid; i.e., judgements scored at or above this numerical point can validly distinguish the presence of auditory responses 95 per cent of the time.

To administer and score an EER-Audio test properly, the scientist who uses this method should either be a good EEG technician or have the help of a good technician in operating the EEG instrument. This granted, in keeping with the familiar "Do it yourself" tradition which seems to have swept other fields, we offer a step-by-step formula for administering, interpreting, and evaluating an EER-Audiogram.

## "How to Make an EER-Audio Test"

### METHOD OF PRESENTATION

A. *Preparing the Patient*: This part of the test involves two processes—first helping the patient (or, in the case of a child, his parents) to understand the test, and secondly, getting him physiologically "ready." The first is fully as important as the second, since EEG is so remote from the everyday experience of most patients. It is helpful, for example, if the patient (or parent) understands that the electrical current runs *from* him *into* the machine, not vice versa. Indeed, he should be fully assured that nothing is done to him by the equipment, but that all activity is the other way around. Patients have been known to undergo the test in the expectation that their brains would be damaged in the testing. It is also wise to reassure the patient about the kind and extent of information which the

machine can pick up. Owing to a general reverence for the occult powers of electronic equipment, patients may believe that some kind of direct transcription of thought processes will take place.

Having calmed his fears, we now can give him the sedation which he must have to be physiologically receptive. For these studies, we have found the use of mild sedation indispensable. Clearly, since what we are hoping to discriminate is an "arousal" change in activity of the nervous system, the patient must not be aroused to begin with, or no change can be observed. We wish to create in the subject the basic "level of awareness" that will provide maximal contrast for the auditory responses.

Although it might be possible to secure voluntary repose in some subjects, medication must be used for this group as well, since repose is a transition state, and difficult to maintain. Moreover at this level, accommodation to stimuli is swift. Stimulus presentations would have to be widely spaced to allow the subject to return to a receptive state. In a sound-accommodated subject, even behaviorally visible responses might fail to appear as cortical responses on the record. Within the fairly exacting time limitations of most hospital or clinic schedules, the time wasted in stimulus-spacing for reposed subjects would be uneconomical.

Secondly, repose states, even if sustained, do not fully answer the need for a maximally stable background of C.N.S. activity, against which the responses can be seen. Some moderate stages of sleep are preferable for this purpose. Sleep is a thalamically controlled and primitive pattern of function, common to all types and ages of people, and much more uniform in its expression than are the varieties of waking states. Most individual differences in responding can be attributed to dominant cortical functions; this source of idiosyncratic response is reduced in sleep, when the higher cortical centers abdicate in favor of thalamic regulation.

Finally, sleep also provides us with the opportunity to elicit one particular, well-studied, "standard" form of arousal reaction—the "k complex" to arousal. This response is essentially universally present in normal subjects,[2] and is available primarily in moderate sleep levels. This easily recognized response, seen against the background of the

generally more uniform activity of the sleeping state contributes to greater consistency of interpretive results.

In sum, the sedative gives us three advantages: 1) ease and economy of presentation, 2) greater uniformity of the physiological state, and therefore of the background activity, and 3) a nearer approach to standardization of the response.

With regard to the sedative agent employed, we have used several sedatives since our first report[4]—seconal, paraldehyde, chroralhydrate, pentathol sodium, and various attaratic agents. All of these are effective and useful, providing the pharmacologic action is not so profound as to prevent arousal. Recently, we have had best or most universal success with Attarax® (at 1-2 mgm / .045 kilo. or 1.0 lb of body weight), and seconal (1 mgm / .045 K.). Both are given orally (elixir or pills), before the test is to be administered. The action seems to be that the Attarax reduces the anxiety or tension to such an extent that the sedating effect of the seconal can work unimpeded. If great anxiety is present, the Attarax may be given at home before coming to the hospital. Although EEG tests are frequently run by non-medical staff it is essential that these medications be controlled by a physician. An example of the type of clinical situation which demonstrates the need for medical supervision is the frequent coincidence of delayed resistance, or aberrent responses, to medications. Once the drug has "reached" the child, he may suddenly react profoundly. There is also the occasional child who develops laryngospasm with sedation (about 1 child in 250), and who may need prompt attention. Since most EEG laboratories are established either in hospitals or doctors' offices, the requirements for medical attention can easily be met.

B. *Administration.* After the sedative is administered electrodes are applied. We use silver discs, covered on the bottom with bentonite paste. They are held in place with one inch squares of adhesive tape. The scalp is first scrubbed with alcohol and then the wet paste is firmly pressed onto the clean scalp surface, so that it adheres well (as a test, the operator can lift one electrode; if the contact is good, some of the paste should cling to the scalp.). If the paste-scalp contact is inadequate, and high resistance develops, the corresponding channel tends to pick up 60-cycle per second artifacts from the local electrical circuits (lamps, audiometer, etc.). The contact of the

paste and the electrode is also vital to a readable record, free of artifact. The procedures necessary to insure this contact are, as in the scalp-paste adherence, a clean surface (of the electrode, in this case), and wet paste. The artifacts which identify a loose paste-electrode connection tend to be sharp, angular waves, with steep, straight fronts. If such an artifact is compared with the calibration pattern, it will be found to have the same basic form. (For a more precise, detailed account of instrumentation, see reference 11.)

For the location of electrodes, we have used a system of placement which attempts to offer both localizing possibilities for the skilled electroencephalographer, and also a maximum of detectable change for a reader seeking the auditory response. Six electrodes are placed near the vertex, six are placed around the area of the "hat band" and an electrode on the left temple is earthed. The vertex leads are:

Left and right premotor, No. 2 and 12, 2 cm on each side of midline and in the frontal plane passing 2 cm anterior to the vertex.

Left and right motor No. 3 and 13, 2 cm on each side of midline in frontal plane passing through the vertex.

Left and right parietal, No. 4 and 14, 2 cm on each side of midline and on the frontal plane passing 2 cm behind the vertex.

The "hat band" positions are:

Left and right frontals, No. 1 and 11, on the forehead.

Left and right temporal, No. 6 and 16, 1 cm above the pinna of the ear.

Left and right occiptal, No. 5 and 15, 1 cm above the occipital protuberance and 3 cm lateral to the midline.

The electrode combinations are 2-1, 12-11, 3-6, 13-16, 4-5 and 14-15. Electrodes 4-5 and 14-15 show the least evidence of auditory responses and may be omitted

The "k" patterns, central humps, and spindles, which all tend to be localized in the vertex area, are prominent in electrodes 2, 12,

3, 13, 4 and 14. Such EEG phenomena appear in phase in all channels. Any EEG feature in a single channel which is local or out of phase with the majority other channels probably arises from the "hat band" electrode for that channel.

Although the plotting of the EER-Audiogram is based on responses to tone, each patient is given a preliminary period of testing before the tone presentation to ascertain his general sensitivity, and the nature of his responses. This general-arousal testing consists of: 1) a series of clicks, made by snapping a metal toy cricket, for a double, staccato sound,* at different fixed distances from the subject's ear (ranging from 25 to 30 feet to 3 feet). The clicks are followed by 2) a series of vibrations—each vibration stimulus consisting of a moderately intense blow on the leg of the cot or chair in which the patient reclines. These explorations furnish specific information about the subject's responsiveness in areas closely related to tonal-reception. But more importantly, when interpreted in conjunction with the EER-Audiogram, and the basic EEG pattern, they help to point up discrepancies in these related functions. A tentative classification of syndromes within the general area of disturbed communications, based on differential response to clicks, vibrations and tones (plus the basic EEG-rating) is outlined in Table I. If as a result of this preliminary testing, the subject is near wakefulness, it may be necessary to allow the patient to regain a sleep state before proceeding with the pure-tone presentations.

In the EER-test-proper, selected pure tones are presented in a randomized pattern of varying intensities, interspersed with "no stimulus" presentations. The latter are intervals in which the signal marker is switched on and off, exactly as in tone-presentations, but no stimulus is concurrently presented to the subject. While the record is being run, the technician writes the intensities of the presented tone in the space over the signal mark for each stimulus period, or writes "N.S." for each no-stimulus period. These data, identifying the stimulus, are recorded in red ink or pencil, so that the subsequent reader, wearing red goggles, such as those used for dark-adaptation by radiologists, will not have this information to bias his judgement

* The click may be produced by any electronic circuit with any degree of sophistication providing the requirements are met of a sharp-fronted, short-lasting burst of relatively broad band noise which will stimulate the entire basilar membrane briefly.

TABLE I

EER-AUDIO PROFILES OF FAMILIAR CLINICAL GROUPS

| PROBABLE DIAGNOSES | EEG-DATA | | | |
|---|---|---|---|---|
| | BASIC EEG PATTERN | EER TO CLICKS | EER TO VIBRATION | EER TO TONES |
| Normal, or Psychogenically Deaf | Normal | Normal | Normal | Normal |
| Periferally Deaf | Normal | Decreased | Normal | Decreased |
| "Aphasoid" Child | Normal | Absent | Absent or Normal | Mild Decrease |
| "Brain-damaged" | Abnormal | Normal | Normal | Normal |

as to whether a response has in fact taken place. Over each signal mark, then, there will be recorded in red some such information as: "3000 L. 20" (indicating a stimulus of the frequency 3000 cps, presented to the left ear, at a sensation level of 20 decibels), or else "N.S." (signifying a no-stimulus period).

Each of the factors in presentation, duration of stimulus, interval between stimuli, etc., can potentially modify a response. A systematic study of optimal settings of these factors is in process now. But preliminary trial-and-error observations indicate that the most readable records at present are those in which one presentation of either stimulus or no-stimulus is made at any selected interval greater than 25 seconds, and in which the duration of the stimulus (or no-stimulus) is approximately 4 seconds ($\pm$ 1 second).

Since we want to use a statistical method to evaluate our results, we need to utilize a pattern of presentation of tones and "no stimulus" signals, which readily yields to statistical interpretation. The most appropriate procedure, at our present level of understanding of the various tone dimensions, is that of a randomized pattern. We achieve this by preparing a deck of cards with the desired stimuli present in the desired quantity. The deck is well shuffled and by drawing from the top of the deck, every 20 to 40 seconds, and presenting the indicated stimulus a random series is accomplished. If an exact interval of 30 seconds is used there is the possibility of a sequence of tone presentations so long that time conditioning results. Varying

the interval irregularly between 20 to 40 seconds will obviate this problem. We place in the deck 8 cards for each of the categories given below and then add one "no stimulus" card for each "stimulus" card.

### UNDERSTANDING THE RECORD

A. *Reading the Tracings.* There are certain preparatory attitudes which will help an inexperienced reader of the EER-Audio to maximize his correct judgements, and to gain confidence as he gains

DISTRIBUTION OF RANDOM "DECK" OF STIMULUS PRESENTATION CARDS

*Frequency* (c.p.s.)

| Sensation Level | 500 | 3000 | 6000 | |
|---|---|---|---|---|
| −10 | 8 | 8 | 8 | (These values are chosen |
| +10 | 8 | 8 | 8 | to cover the low and high |
| 30 | 8 | 8 | 8 | end of the speech-range |
| 50 | 8 | 8 | 8 | frequencies, and the very |
| 70 | 8 | 8 | 8 | high frequencies.) |
| Total No. of cards | 32 | 32 | 32 | = 96 |

96 stimulus cards + 96 NS cards = a total deck of 192 cards.

experience. It is necessary to understand, first, that the presence in the EEG pattern of any change of any type or form may reveal information relative to auditory activity. At the present time, there are no known "templates" (or ideal, general stencil-forms) for the electrical patterns resulting from auditory stimulation, in humans. Even if one such template were known, this by itself would not necessarily solve the problem for the inexperienced observer, for there must certainly be a number of different magnitudes, and possibly

even different forms, of activity which might represent an auditory response. The reader who wishes to measure, by EEG, the information presented to the cortex by the sensory limb of the auditory system must be alert to any and all possible signs. What an untrained but earnest observer really needs is some index of EEG change in response to sound, which is sufficiently definitive so that he can determine whether the post-stimulus pattern he is looking at does or does not constitute a response. To be useful, such a guide must enable the reader to make this determination dependably enough to satisfy the clinical needs of his situation.

Several procedures for the actual reading process were tried before the current one was adopted. The first few records were read with the stimulus properties designated over the signal mark, and known to the reader. Soon, however, we felt the need for some control against the distortion of biased expectancy on the part of the reader.

A dozen-or-so records were then read in which both stimulus dimensions and the signal tracing itself were given in red, so that the time of stimulation as well as its character were obscured by the reader's red goggles. By this method, the reader only knew that somewhere in each 20 seconds of record (which was the inter-stimulus interval then used) there was a brief period in which stimulation of some intensity ($-10$ to $+90$ db), or a no-stimulus period, had been presented. He had then to discover the response by examining each segment of the record minutely. Though unbiased, this method was extravagant of reader-time.

However, with greater experience in reading, the criteria for discriminating a response became more uniform and objectified. We were able to make judgements on the basis of recognizable, describable characteristics of the tracing. At this point, we adopted the method described earlier of writing the dimensions of the stimulus in red, over the (black) signal marker, thus leaving the time of stimulation visible. By this present method—visible signal, unknown stimulus—we are able to study and interpret an additional characteristic of the response, unavailable in the totally "blind" reading; the *latency* of the response, defined as the interval between stimulus signal and EEG-change.

Thus, by randomizing the stimuli presented to the subject (see discussion of presentation pattern, above), we are able to minimize subject-expectancy, or the "conditioning" of a response. By the modified "blind" reading of the record, we can also remove reader-expectancy as a determinant of the decision that a response has occurred. That is, the subject cannot be "set" to respond to stimuli of a given intensity or a given presentation rate, since the random presentation of varied stimuli, interspersed irregularly with no-stimulus periods, does not allow the formation of a learnable pattern. The subsequent "blind" reading of the record obliges the reader to reach his decision as to the presence or absence of a response solely on the basis of objective characteristics of the EEG record, without modifying his judgement by information about the presence and intensity of a stimulus tone.

This device is not used to trick the person reading the record, or to test his accuracy. We recognize that this central nervous system whose activity we are watching is continually responding to various stimulation—some of which may be the tonal stimuli we are presenting, but most of which are unknown to us, the readers of the record. What we wish to be able to judge is not whether the subject is responding (for we know he is), but whether he is responding *to the particular stimuli we are offering.* Consequently, we must learn to recognize the characteristics of response to a tone-stimulus, and must be able to demonstrate by statistical methods that these indices reliably differentiate the background activity from the responses to those stimuli which we define as relevant (i.e., those which we present).

Our reasoning, in the use of the method described, is as follows: The "no stimulus" periods randomly scattered through the record are equivalent to random samples of the background activity of the particular brain we are observing, since no stimuli have been introduced to alter the ongoing processes. Thus, by comparing our reader-decisions for these no-stimulus periods to the decisions made when a tonal stimulus accompanies the signal mark, we can evaluate our efficiency in distinguishing response from background.

B. *Scoring the Responses.* Our scoring system assigns an arbitrary numerical value to each of the EEG changes we have selected as characterizing an auditory response. The segment of the record tape between the "on" and "off" signal marks is given a score, based on

the number of changes observed. Thus each such segment of record yields a score. The score-values obtained by combining all such scores for each of the stimulus categories (each frequency/intensity category) can be compared with scores for other stimulus categories, and with the scores assigned to segments in which the signal mark was not accompanied by a stimulus. The average value assigned to the periods of "no stimulation" must be significantly different from the averages for tone presentations, if we are to consider our judgements as valid.

TABLE II

FEATURES USED TO IDENTIFY AN EER TO A FOUR SECOND PRESENTATION OF A PURE TONE

(Scores in Parentheses)

| ON (0 - 1.5 sec) | CONTINUOUS (2.0 - 4.0 sec) | OFF (4.0 - 6.0 sec) |
|---|---|---|
| K complex (3) | Appearance of alpha activity and or muscle potentials (4) | |
| Voltage reduction or frequency change (2) | Absence of spindles expected in this segment (2) | |
| | Voltage reduction or frequency shift (2) | K complex less than with ON or marked pattern change (2) |
| Minimal change (1) | Minimal change or a late K complex (1) | Return to pre stimulus pattern or voltage reduction (1) |

Appearance of a spindle of 12-14/sec waves is never scored as a positive feature. If there is no evidence of any of these features that segment of record is rated as one (1).

Table II is a condensed summary of the EEG features looked for and scored in any segment of record marked by the signal.

There are four basic forms of change: 1) voltage increase, 2) voltage decrease, 3) frequency changes, and 4) the total configuration, or changed organization of the pattern.

Figure 2 gives examples of these various features in EEG patterns actually obtained, from different patients. The "scores" for these

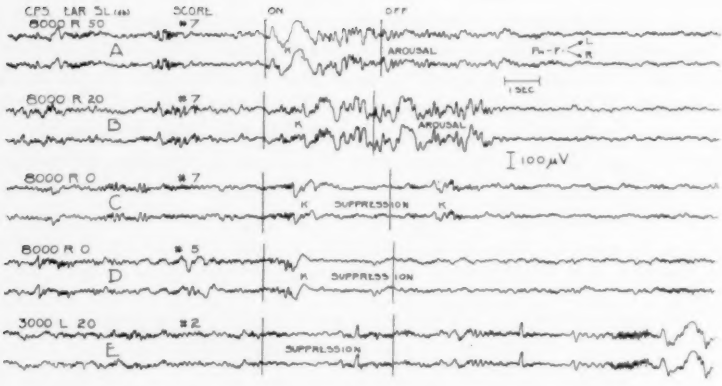


Fig. 2.—Samples of traces from premotor (PM) to frontal (F) electrodes (2-1 and 12-11), scored as follows:

A. 8000 cycles per second to right ear at sensation level (S.L.) of 50 db. Features: 1. Short latency K (score 3), followed by 2. Full arousal (score 4). Total Score = 7.

B. 8000 cps, R ear, at S.L. 20 db. Features: 1. Longer latency K, (score 3), followed by 2. Arousal (score 4). Total Score = 7.

C. 8000 cps, R ear, at S.L. 0 db. Features: 1. Longer latency K, (score 3), followed by 2. Suppression (score 2), and 3. K "off effect" (score 2). Total Score = 7.

D. 8000 cps, R., at 0 db. Features: 1. Long latency K (score 3), followed by 2. Suppression (score 2). Total Score = 5.

E. 3000 cps, L, 20 db. Features: 1. Long latency suppression (score 2); 2. No other sign of response. Total Score = 2.

(All traces show similar level of sleep at onset of stimulus. Variations in responses are related to intensity of stimulus and other undescribed factors in the situation and the patient.)

features are given below each pertinent section of the trace. We do not believe that these are the only and final indices of the responses we are studying. They are the ones we have been able to recognize analytically so far. Any and all observable fluctuations in these electrical "wiggles" might contain information about the auditory system, and any observer may develop indices which allow him to refine his decisions as he goes. In this laboratory, we have set as a current research goal the more precise description of these EEG modifications, and their relationships to levels of sleep, to the varieties

of stimulus dimensions, and to all other relevant parameters of the experimental situation.

However, until we have progressed far enough in these studies to formulate specific predictions for the influence which each presentation factor exerts over the resulting EEG response, we must content ourselves with establishing the fact that the presentation of a tone does affect the total EEG pattern in detectable ways.

C. *Evaluating the Results.* We define the EER-Audio "threshold" as: *the lowest sound intensity which consistently evokes a statistically verifiable response.* To estimate this threshold, we statistically compare the scores given for "no stimulus" segments with those given for the tone stimulus segments of the record. Our formula is based on the non-specific null hypothesis that these sets of EEG-segments are samples from the same population of segments, and that the scores assigned to them could only differ on a chance basis. Probability theory allows us to assume that in successive samples from the same population, the mean values( in this case, scores) of the samples will not differ significantly. On this assumption, the actual mean values obtained from scores for the "no stimulus" and "tone stimulus" samples can then be compared by a simple T-test:

$$(1) \qquad t = \frac{X_1 - X_2}{Sp\sqrt{\frac{1}{N_1} + \frac{1}{N_2}}}$$

$X_2$ = mean of scores for "no" stimulus segments

$X_1$ = mean of scores for "stimulation" segments

$Sp$ = pooled sum of squares of deviations from the mean and

$N_1$ = number of observations with "stimulation"

$N_2$ = number of observations with "no stimulation"

Since in our cases so far the pooled sum of the squares of deviations is less than 1, this factor can be effectively dropped from the formula (literally, by substituting the value "1" for it).

The critical value of t, for the 95% confidence level, with a total N ($N_1 + N_2$) of more than 20 observations, is 1.8. To ascertain the value at which our "tone stimulus" scores reach significance, we

can substitute the empirical results of any particular scored record for the terms of the formula (1) as follows (solving for $X_1$):

$$(2) \qquad 1.8 = \frac{X_1 - X_2}{(1)\sqrt{\frac{1}{N_1} + \frac{1}{N_2}}}$$

$X_2$ = value given by mean of scores assigned to "no stimulus" observations.

$N_1 + N_2$ = total number of no-stimulus observations, plus the number of observations in the set of tone-stimuli being compared ($N_1$ = 5).

In our experience, $X_2$ usually produces a value from 2.0 to 2.5, setting the critical value for $X_1$ at 2.8 to 3.3. That is, if the mean scores for the tone-stimulus segments of the record exceed the mean score for no-stimulus segments by at least 0.8, we can be 95 per cent confident that these two means are from different populations, which is another way of saying that we can distinguish responses from background activity 95 per cent of the time. The reliability of these findings has two distinct components, namely, the consistency of the subject over several testing situations and the consistency of the reader. Consistency of subject is so complex a problem that a separate research project has been undertaken to answer it. We do, however, have reliability measurement for reader consistency based on several scorings of the same record by the same judge and independent scoring by two judges using the same scoring system. These results are given in Table III.

For added conviction, the reader can verify the statistical results by checking certain common-sense correlations that should appear in the data themselves. Reason tells us that when we compare tone-presentations at −10 decibels with the no-stimulus scores, the differences in these values will be less striking (or less frequent) than the disparity we might expect to find in comparing the same "no stimulus" scores with those given for tones at 30 or 50 db levels. As the intensity-levels of presented tones increase, the ratio of tone scores/no stimulus scores should similarly increase. This progression would

TABLE III

RELIABILITY OF READER-RATINGS

A. *Stability*: Stability of ratings is expressed by the product-moment correlation between a single judge's ratings on two fairly widely-spaced readings (3 months - 1 year) of the same subject's records:

| | |
|---|---|
| *Patient 1*: Male, six years. Referred for evaluation of hearing loss. Autistic. (106 responses scored) | $r = .601$ |
| *Patient 2*: Female, 3 years. Referred for differential diagnosis of delayed language development. (90 responses scored) | $r = .605$ |
| *Patient 3*: Female, 4 years. Referred for differential diagnosis of delayed language development. (158 responses scored) | $r = .466$ |
| *Patient 4*: Male, 60 years. Normal subject. (202 responses scored) | $r = .800$ |

B. *Consistency*: Consistency of ratings is expressed by the product-moment correlation between two judges' independent ratings of the same subjects' records:

| | |
|---|---|
| *Patient 1*: Female, 45 years. Referred for evaluation of hearing loss, based on organic and psychic pathology. (52 responses scored) | $r = .463$ |
| *Patient 2*: Male, 2½ years. Referred for differential diagnosis of delayed language development. (111 responses scored) | $r = .730$ |
| *Patient 3*: Female, 4 years. Referred for differential diagnosis of delayed language development. (158 responses scored) | $r = .802$ |
| *Patient 4*: Male, 60 years. Normal subject. (103 responses scored) | $r = .759$ |

reflect the increasing detectability of signal in noise as the intensity of the signal (presented tone) rises.

In general, our studies so far support this expectation, with certain notable and consistent exceptions. Dr. William Hardy[9] has described for the EDR peculiar "notches" in the steadily rising function of identifiability of tones of increasing intensity. Comparing notes with Dr. Hardy, we find parallel "gaps" in the otherwise steady progression of response-with-intensity. Since we do not have repeated studies on the same subjects (either our normals or our communi-

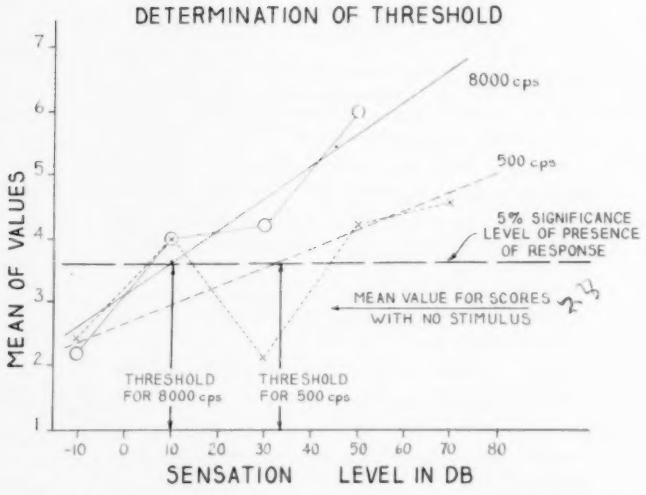


Fig. 3.—Graph shows cortical thresholds for two subjects, using two tone frequencies (8000 cps for subject A—continuous line, and 500 cps for subject B—broken line). The "no stimulus" (or *chance*) value is indicated by an uncompleted horizontal line, with arrow pointing to score value of 2.8. The level of "significant response" is represented by a dashed horizontal line, at the score value of 3.6.

Both the raw score profiles (irregular, jagged point-connections) and the 'smoothed' profiles (continuous, sloping lines) are given for each subject.

Thresholds in each case are represented by perpendiculars dropped from the point where the smoothed profile crosses the significant response level (for Subject A, 10 db; for subject B, 33 db).

Graph demonstrates the frequently-encountered "30 db-dip," accentuated in Subject B (500 cps).

catively disturbed subjects), we cannot say whether these are individual idiosyncrasies, experimental artifacts, or consistent characteristics of the human auditory system. However, these dips in the auditory profile do not change our definition of a threshold, as previously stated. The EER-Audio method yields an easily interpretable graph of the subject's auditory acuity, as measured at the cortex. To obtain such a graphic outline, the mean scores of tone-presentations (represented in ascending magnitude on the vertical plane or ordinate) are plotted against increments of increasing intensity of presented tone

(placed along the horizontal dimension, or abscissa). Next, a line is drawn parallel to the abscissa, at the vertical height represented by the mean of "no stimulus" scores. The resulting graph will have the general appearance of Figure 3.

If a smoothed curve is drawn connecting these points, we can then mark off on that curve the point representing a value of 0.8 greater than the noise-level. The corresponding intensity of tone (that point on the abscissa which falls directly under this value) may be taken as a cortical threshold for the tone-frequency.

There is a small but significant percentage of subjects (about 15 to 20 per cent) who fail to yield significant responses or threshold values at any intensity level. Since we believe at present that not more than one case in 1000 is actually handicapped by such severe deafness, or failure of arousal, this group represents a temporary limitation of the present method. Repeat studies are being undertaken on such cases, in the hope that fuller understanding of these failures may give us increased insight into the processes underlying the EER-Audio.

It is most valuable for the novice in the use of this procedure to reassure himself by studying some five or six known, normally communicating subjects of various ages to see how well the EER-Audio thresholds he obtains parallel the general trends shown in these subjects by standard audiometry.

## SUMMARY

A method is suggested for the administration, reading, and interpretation of electroencephalic responses to sound (the EER-Audio test). It is felt that the EEG taps a part of the hearing act which none of the currently familiar audiometric tests is able to reach. In addition to the independent usefulness of this assessment, the EER-Audio data also enrich the interpretive significance of other audiometric test results, by adding a reading from another level of the hearing mechanism. The differential results of standard audiometry, EDR, and EER-Audio present a comparative study of the amounts of auditory information available at each of several points on the auditory pathway, and permit us to distinguish objectively the clinical entities associated with each locus of loss.

The two principal deterrents to general use of the EER-Audio are discussed. These are felt to be:

1) The high degree of skill and training commonly thought to be required for interpreting the record.

2) The need for standardization of the test. The first difficulty is easily resolved, by pointing out that the detection of an auditory response within the EEG pattern does not depend on the understanding of the brainwave patterns. The reader of the EER-Audio simply learns several pattern changes which have been found to accompany auditory stimulation and then searches the designated segments of the EEG record for the occurrence of these responses.

A preliminary answer to the need for standardization is also given. The authors have developed a method for validating their results by reference to the auditory stimuli presented. Through the use of the statistical procedures described, it is possible to construct a cortical auditory threshold with any desired level of confidence. Estimates of interpreter-reliability, based on re-interpretations by the same reader, and on independent interpretations by different readers, are appended.

3322 S. Dearborn St.

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XLIX

# THE OTOTOXICITY OF KANAMYCIN

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(by invitation)
NEW YORK, N. Y.

Kanamycin is a recent major addition to the useful but unruly family of basic streptomyces antibiotics, which includes not only streptomycin and its reduction product dihydrostreptomycin, but neomycin and viomycin as well. Kanamycin was discovered in 1957 by Hamao Umezawa of the National Institute of Health in Tokyo, in the course of a program of screening new, water-soluble, basic antibiotics produced by actinomycetes.[1] Because of its broad antimicrobial spectrum, favorable toxicity showing in mice and relative ease of production and purification, it was selected for special study. The rare strain which produced it was assigned by its discoverer to a new species, *Streptomyces kanamyceticus*.

Paper chromatography of the early kanamycin filtrates showed the presence of two active components. The major component, which was called kanamycin A, was hydrolyzed by Cron and associates[2] into three fragments, by boiling in 4N hydrochloric acid for 15 minutes. Two of these products proved to be amino sugars, 3-D-glucosamine and 6-D-glucosamine, and the third a hydroxylated base, 2-desoxystreptamine, joined to the aminohexoses by glycosidic linkages. The structure bears a strong resemblance to streptomycin, and especially to neomycin.

Kanamycin exhibits bactericidal activity against a variety of Gram-positive, Gram-negative and acid-fast organisms.[3] The staphylococci and bacilli tend to be quite sensitive, the streptococci and

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clostridia relatively insensitive. It is active against some strains of *Pseudomonas* and *Proteus*. S. *aureus* and *E. coli* develop resistance to kanamycin in vitro more slowly than to streptomycin, but the resistance of mycobacteria may develop rapidly. Staphylococci resistant to many of the commonly used antibiotics may be sensitive to kanamycin. Kunin and Finland[4] found cross resistance of coliform organisms among kanamycin, neomycin and paromomycin, but the cross resistance did not extend to streptomycin.

A pharmacological investigation of kanamycin in animals by Tisch, Huftalen and Dickison[5] showed that kanamycin was well absorbed when given by the subcutaneous or intramuscular route, but not by the oral route. It appeared in the cerebrospinal fluid in concentrations directly related to the concentration in the blood. Kanamycin was rapidly excreted in the urine, apparently by glomerular filtration alone. Evidence of kidney damage was seen in dogs receiving 200 mg/kg daily for two to three weeks, and necrotic changes in the renal tubules were revealed at autopsy. The nephrotoxic effect was similar to but not so destructive as that of neomycin. In cats an irreversible vestibular disturbance occurred, and, in rats trained to climb a rope in response to a buzzer, a slight, reversible diminution of hearing. These changes were said to be less severe than those produced by streptomycin and dihydrostreptomycin respectively.

In spite of the favorable showing of kanamycin in the laboratory, mild to moderate nephrotoxic effects have been observed by almost all clinical investigators. Hyaline or granular casts frequently appear in the urine a few days after treatment is begun and tend to persist throughout treatment. Small amounts of albumin may also appear, but rarely does an elevation of the blood nonprotein nitrogen or an oliguria occur.[6]

Short-term treatment with kanamycin usually has no adverse effect on either the vestibular or the auditory system. With prolonged use, as in the treatment of tuberculosis, several instances of hearing loss have occurred, as reported by Bunn and associates,[7] McClement and associates,[8] Donomae[9] and Finegold.[10]

Through the co-operation of Dr. McClement and his associates from the Bellevue Hospital Chest Service, Dr. J. O. Frost, Dr. J. F. Daly and I have had the opportunity of carrying out a study of the

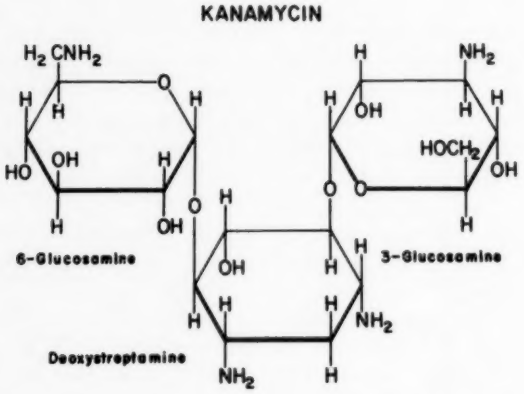


Fig. 1.—The structure of kanamycin A, according to Cron, *et al.* (2).

ototoxicity of kanamycin in tuberculous patients. A preliminary account of this work was given at the Sixth Antibiotics Symposium in Washington, D.C., last autumn,[11] and a further report at the recent Veterans Administration Conference on the Chemotherapy of Tuberculosis.[12]

The first group of 14 patients had all received extensive treatment with the usual antituberculous drugs, including streptomycin and dihydrostreptomycin. Since their organisms were fully resistant to all of these agents, this group of "drug-bankrupt" patients seemed appropriate for a trial of kanamycin. Unfortunately the audiograms of at least seven of them showed varying degrees of perceptive loss, which may have been caused by previous antibiotic therapy. Group I was divided into three subgroups, who received kanamycin 0.5, 1.0 and 1.5 gram daily. The treatment lasted for 120 days, or longer if the patient appeared to benefit from it. Group II consisted of seven patients, none of whom had received previous chemotherapy for their disease. They were given 1.0 gram daily, and treatment was interrupted as soon as audiometric changes occurred. Only one patient in Group II completed the scheduled 120 days of treatment. Group III consisted of 8 patients who were given three grams weekly for 120 days.

The kanamycin supplied to Dr. McClement was stated to consist of kanamycin A, with only 1 to 3 per cent of kanamycin B. Treatment was by the intramuscular route in all cases.

Table I summarizes the dosage of the three groups of patients and indicates the total dose in grams at the time that a disturbance of hearing was first noted either audiometrically or subjectively. Of the 18 patients who showed some degree of auditory impairment, 8 were affected before they had received 60 grams of kanamycin, and 8 more before they had received 120 grams.

TABLE I

DISTRIBUTION OF PATIENTS ACCORDING TO TOTAL DOSE AT ONSET OF AUDITORY DISTURBANCE

| | DOSE | | TOTAL DOSE (GRAMS) AT ONSET OF AUDITORY DISTURBANCE | | | | |
|---|---|---|---|---|---|---|---|
| | GM/DAY | MG/KG | 0-30 | 31-60 | 61-90 | 91-120 | 121-150 |
| I | 0.5 | (10-13) | 0 | 1 | | | |
| | 1.0 | (13-22) | 0 | 2 | 1 | 4 | 1 |
| | 1.5 | (26-29) | 0 | 1 | 0 | 1 | 1 |
| II | 1.0 | (15-25) | 0 | 3 | 1 | 1 | |
| III | 3.0/wk | (14-21) | 0 | 1 | | | |

Thresholds for high frequencies were the first to be affected by the antibiotic. Table II summarizes the results in terms of the hearing loss. In the first group of 14 patients, 2 failed to develop hearing loss, but these were receiving only 0.5 gram daily. In 4 cases where losses occurred, they were confined to the frequencies above the speech range, while in the 8 others the losses extended down into speech frequencies as well.

With Group II, an effort was made to minimize the auditory impairment by stopping the KM treatment as soon as tinnitus was reported or hearing loss was detected. Two patients in this group did not develop any loss, but only one of these completed the full 120 days of treatment. In four patients the losses were confined to the

TABLE II

DISTRIBUTION OF PATIENTS ACCORDING TO FREQUENCIES AFFECTED BY HEARING LOSS

| KM DOSE | | REGION OF HEARING LOSS | | |
|---|---|---|---|---|
| GM/DAY | TOTAL GM | SPEECH FREQ. 500-2000 | HIGH FREQ. 4000-8000 | NONE |
| | | GROUP I: 14 PATIENTS | | |
| 0.5 | 59-61 | 1 | 0 | 2 |
| 1.0 | 112-163 | 5 | 3 | 0 |
| 1.5 | 143-154 | 2 | 1 | 0 |
| | | GROUP II: 7 PATIENTS | | |
| 1.0 | 40-120 | 1 | 4 | 2 |
| | | GROUP III: 8 PATIENTS | | |
| 3 gm/wk | 44-54 | 0 | 1 | 7 |

upper frequencies only, but in one patient to be described below the loss became complete at all frequencies. In Group III only 1 patient out of 8 has shown a loss, and that is confined to the 8000-cycle frequency. In this group the total dose was small in relation to that received by most of the other patients. At the time the evaluation was made (90 days) the total dose was just approaching the critical range at which losses might be expected to develop.

### COURSE OF HEARING LOSS

In Group I, where KM treatment was not stopped as soon as the hearing was affected, the impairment usually became worse with continued treatment. It has remained stationary, however, during a four- to six-month follow-up period. No instances of delayed loss have occurred resembling those after DHSM. In one case (Group II), partial recovery of a relatively mild loss involving all frequencies was seen five weeks after KM was stopped.

Two other cases deserve special mention because of their bearing on the question of the relationship between the ototoxic and the

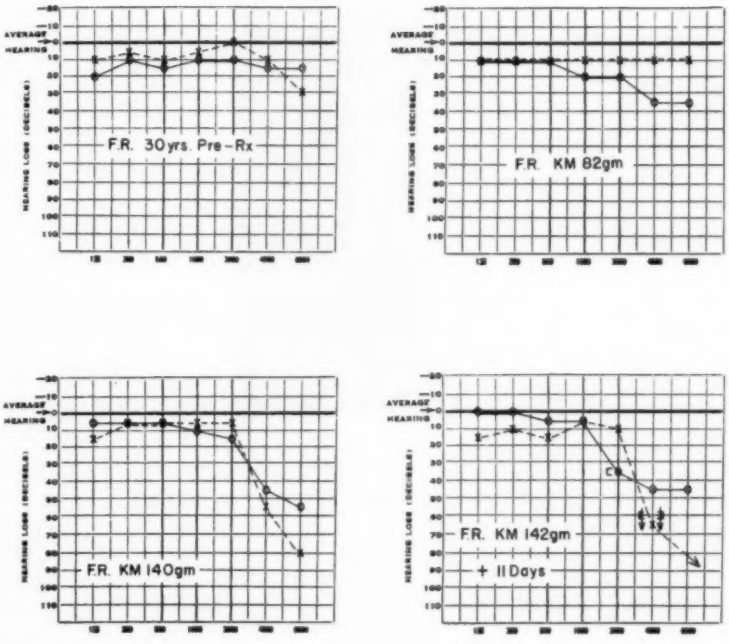


Fig. 2.—Audiogram of a tuberculous patient treated with kanamycin sulfate, 1 gm i.m. daily for 140 days.

nephrotoxic effects of KM. One patient (Group II), whose initial audiogram revealed a moderate, bilateral, mixed type of hearing loss, showed a 1-plus to 3-plus albuminuria before treatment. He was diagnosed as having a mild glomerulonephritis in addition to diabetes, syphilis and pulmonary tuberculosis. After 40 grams of KM (1.0 gm or 15mg/kg daily) his renal function became seriously impaired, with the blood urea nitrogen rising from 18 to 82 mg per cent. At the same time his hearing rapidly deteriorated, so that he became completely deaf during the following three weeks. Unfortunately, we were not in a position to measure the level of KM in the blood, which must have been extremely high. When the patient was able to get up again, he was found to be severely ataxic, although he still showed

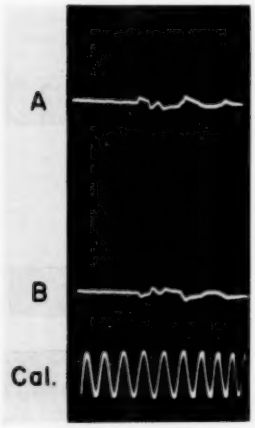


Fig. 3.—Lack of cochlear microphonic (CM) and nerve action potential (AP). Responses to click 100 db above AP threshold, in cat 2143L treated with kanamycin A sulfate, 200 mg/kg/day for 50 days. Cal. 2000 cps, 100 mv r.m.s.

normal responses to stimulation of the semicircular canals. This anomalous disturbance of equilibrium has subsided during the past four months, but he remains completely deaf.

The second patient, who was seen after treatment on another service, was non-tuberculous, but had a urinary infection and a neurogenic bladder as a result of a spinal fracture. He had received 1 gm KM daily for 7 days, and then 4 gm daily for 9 days, making a total dose of 43 grams. During this period he also received 6 gm SM, plus chloramphenicol, penicillin and Gantrisin. Two days after KM was stopped, it was noted that his hearing was impaired, but he could hear words spoken in a loud voice. Four days later he could hear only shouts close to his ear. By the fifth day he was totally deaf, and he has remained so.

The characteristics of the ototoxic effect of kanamycin in man as revealed in this study, may be summarized as follows:

1. Hearing for the highest frequencies is affected first.

2. Tinnitus often precedes or accompanies the onset of hearing impairment, but loss may occur without tinnitus.

3. The loss does not tend to progress after kanamycin treatment is stopped. Delayed loss, such as sometimes occurs after dihydrostreptomycin, has not been seen after kanamycin.

4. Partial recovery has occurred in one case.

5. If renal function is impaired, the loss of hearing may be sudden and complete (2 cases). An anomalous, reversible disturbance of equilibrium was seen in one of these cases.

6. We have no clear evidence that patients with perceptive loss due to dihydrostreptomycin or streptomycin are more susceptible to the ototoxic effect of kanamycin, but this possibility is not ruled out. White and Knight have reported such a case.[13] In two of our cases, however, treatment with kanamycin seems to have sensitized the patient to subsequent treatment with streptomycin. One patient, who showed no impairment of hearing after 59 gm of kanamycin, developed a loss at 8000 cps two months later, after receiving streptomycin 1 gm daily for only thirty days. A second patient was switched to streptomycin immediately after receiving kanamycin 3 gm weekly for four months. He became dizzy and ataxic after only three weeks of streptomycin therapy.

7. Recruitment does not appear to be a feature of the impairment caused by kanamycin. Among seven cases tested by binaural or monaural loudness matching procedures, none showed evidence of recruitment. It appears therefore that in man the kanamycin lesion may not be confined to the organ of Corti, but may extend to the auditory nerve and perhaps beyond.

## OTOTOXICITY IN EXPERIMENTAL ANIMALS

In order to assess the ototoxic potential of a new antibiotic, it is important that more than one species of laboratory animals be used, because of poorly understood species differences in susceptibility to the older antibiotics. We are using cats, guinea pigs and rats in our laboratory study of kanamycin.

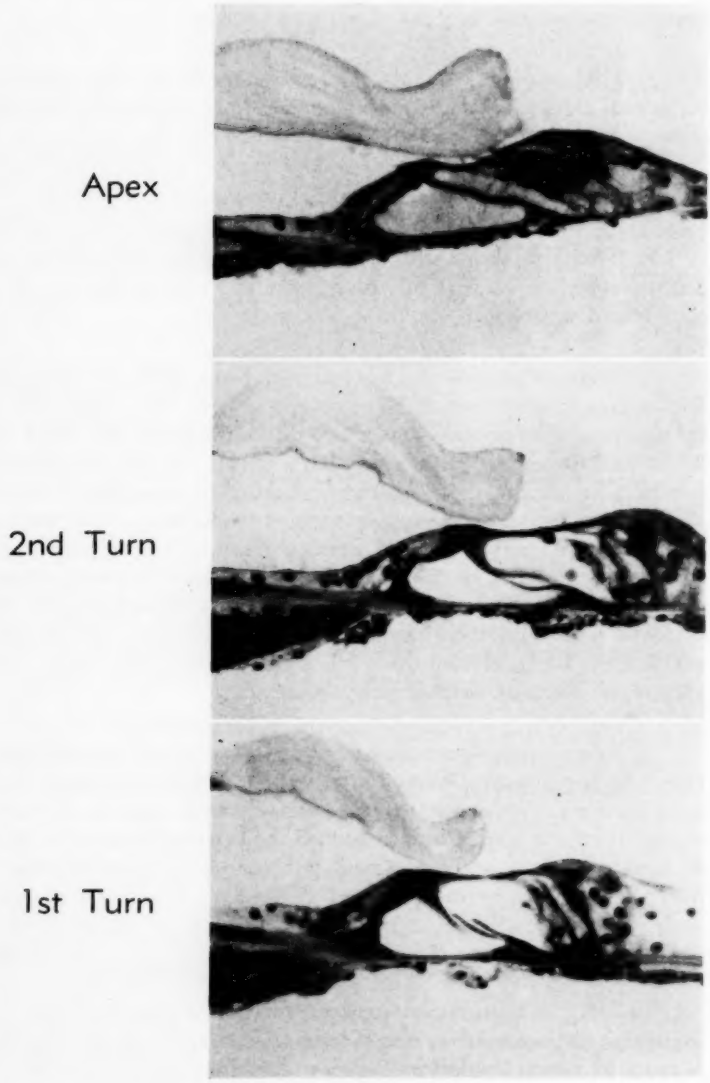


Fig. 4.—Organ of Corti in cat 2144L treated with kanamycin A sulfate. 200 mg/kg/day for 50 days.

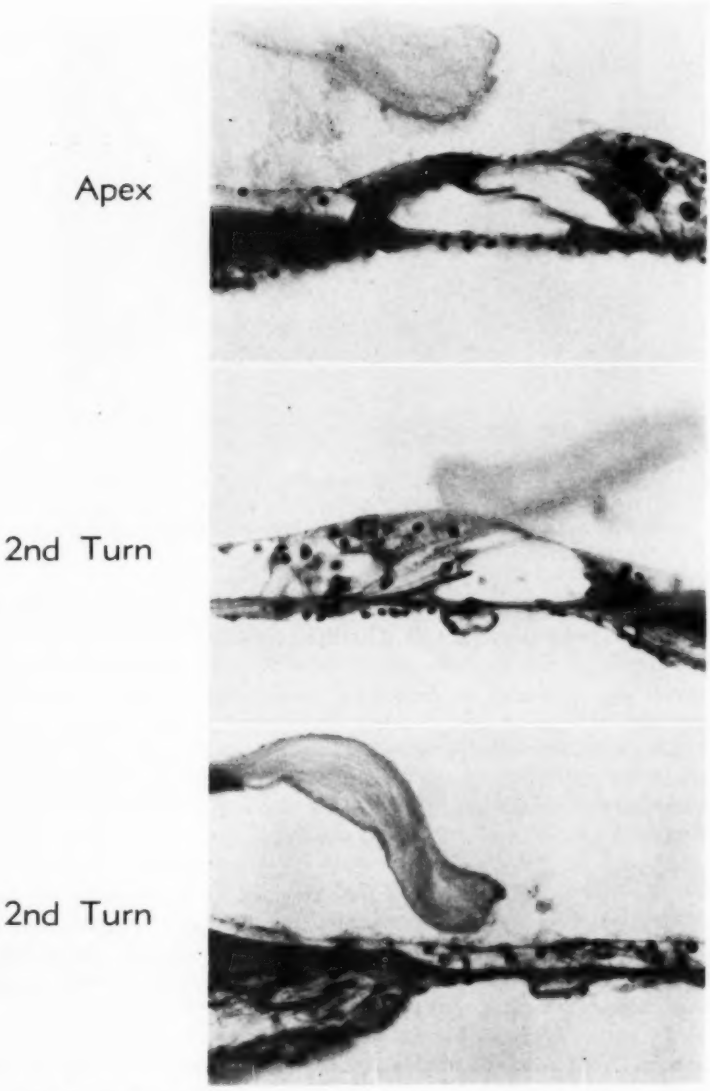


Fig. 5.—Organ of Corti in cat 2151R treated with kanamycin B, 200 mg/kg/day for 30 days.

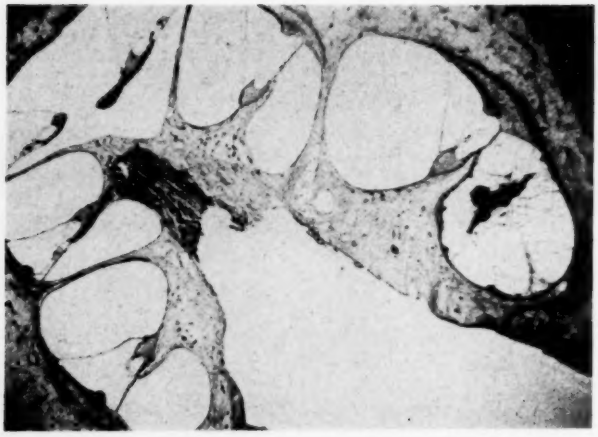

Fig. 6.—Cochlea of cat 2151R, treated with kanamycin B, 200 mg/kg/day for 30 days. No organ of Corti in 1st turn; degeneration of ganglion cells and nerve fibers, including nerve in internal meatus.

Cats were used in a four-way comparison of kanamycin with neomycin, streptomycin and dihydrostreptomycin. After receiving kanamycin 50 mg/kg daily for 75 days, two cats showed evidence of partial loss of hearing as judged by rough attention tests, with little apparent change in the cochlear microphonic and auditory nerve potentials at the round window. Two other cats, treated with neomycin 50 mg/kg daily for 74 and 75 days respectively, showed an apparently complete loss of hearing by the attention tests and a complete lack of cochlear and neural potentials.

At 200 mg/kg, two cats that received kanamycin for 68 and 75 days respectively showed a severe but not quite complete loss of both types of potentials. Two other cats that received similar treatment with dihydrostreptomycin showed normal reactions to sound and auditory potentials of normal amplitude.

So far as the vestibular system is concerned, kanamycin has shown itself less ototoxic than either streptomycin or dihydrostreptomycin. Cats receiving kanamycin 400 mg/kg daily showed ataxia

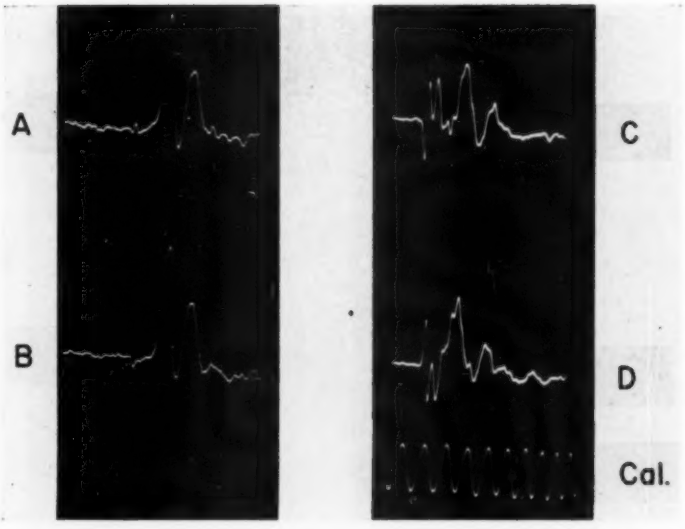


Fig. 7.—A, B: Selective depression of CM with retention of AP in KM-treated cat 2146. Note reversal of small CM component between A and B. C, D: Response of normal control cat 1969 to click of same intensity (50 db above threshold for AP). Cal. 2000 cps, 100 mv r.m.s., applies only to C, D. Gain for A, B was approximately twice as great.

and loss of response to rotation after 21 and 24 doses. Other cats receiving kanamycin 200 mg/kg daily showed no vestibular disturbance during 50 days of treatment. With dihydrostreptomycin 200 mg/kg daily the typical signs appeared after 29 and 42 days; with streptomycin 100 mg/kg daily, after 23 and 24 days.

Kanamycin A sulfate has been used to treat four cats at 200 mg/kg daily for 50 days. At the end of the period of treatment, three showed complete loss of the attention or startle response to intense noise at a level which makes a normal cat retreat in fear, and the fourth gave a response of questionable reliability to noise 50 db above his control threshold for the attention response. The first three animals showed no microphonic response, while the fourth showed a maximum response of less than 10 microvolts, in contrast to the

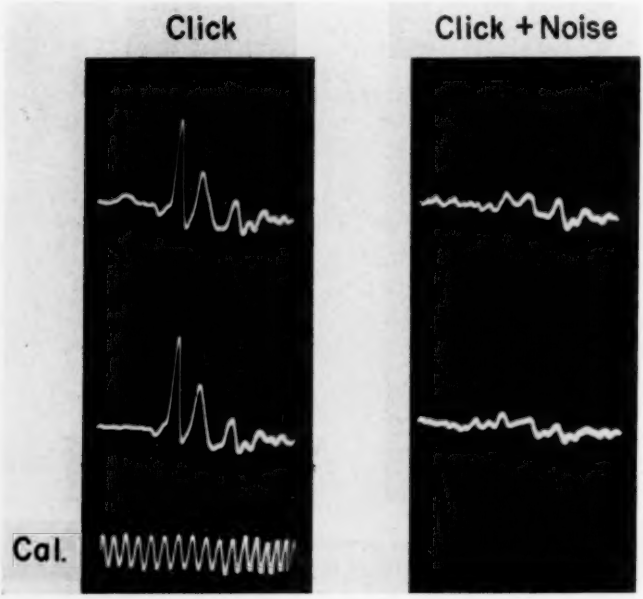


Fig. 8.—Masking of responses to click 100 db above AP threshold, showing that response consists almost entirely of AP. Cal. 2000 cps, 100 mv r.m.s.

normal maximum of 800-900 microvolts at the round window. In all cats the action potentials in response to clicks were of very small amplitude.

Kanamycin B base was used to treat two cats at 200 mg/kg daily for thirty days. Both animals still showed an attention response to noise at the end of treatment, but they were deaf 12 days later when cochlear potential measurements were attempted. Neither showed any cochlear potentials whatever in response to clicks or tones.

Thus far, histological examination of the cochlea has been carried out in only a few of these animals. In one of the cats that received kanamycin A, the external hair cells are missing throughout

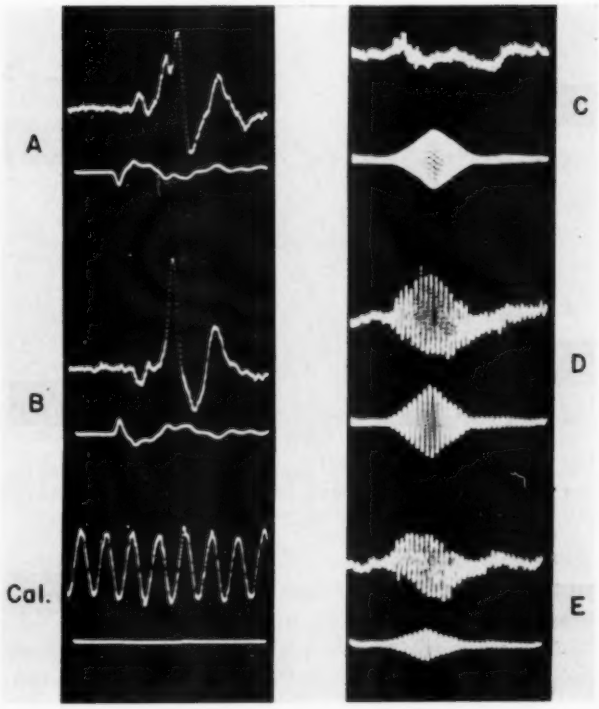


Fig. 9.—Responses of cat treated with viomycin, 100 mg/kg/day for 20 days. A, B: clicks 50 db above AP threshold. C: 8000 cps pulse; D, E 4000 cps pulse, showing presence of summating potential. Upper trace RW response, lower trace microphone. Cal. 2000 cps, 100 mv r.m.s.

the first and second turns, but near the apex the nuclei are visible and hairs can be seen extending into the tectorial membrane. The internal hair cell nuclei are absent in all turns. The cells of the spiral ganglion are present, but the nuclei are pyknotic and the cell bodies appear shrunken.

Much greater destruction is seen in the cats treated with kanamycin B. The organ of Corti has disappeared in the basal turn. In the second turn it is represented by a flattened layer of undifferentiated

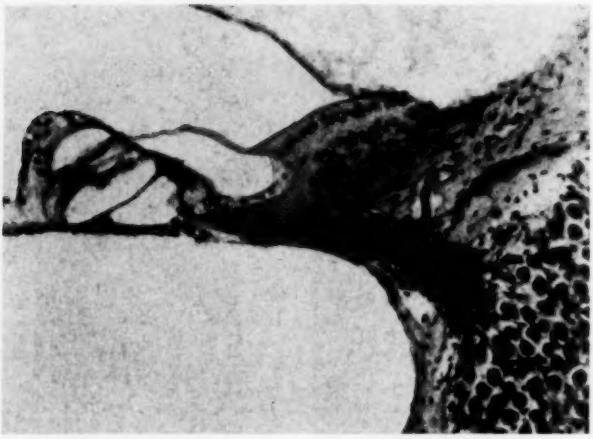

Fig. 10.—Guinea pig 163, 3rd turn, kanamycin A sulfate 400 mg/kg/day for 44 days. Nuclei of internal hair cell and of one external hair cell are present. Nerve fibers and spiral ganglion cells appear normal.

epithelial cells. Ganglion cells and nerve fibers are absent except in the upper part of the second turn and above. Only fragments of the degenerated nerve remain in the modiolus. A further curious feature of this ear is the presence of a calcified body in the scala tympani of the lower portion of the first turn.

In other cats treated with kanamycin in lower doses or for shorter periods of time, selective depression of the cochlear microphonic potential (CM) has occurred, leaving the action potential (AP) well preserved. It is reminiscent of the selective depression of CM already reported with streptomycin, and in contrast to the effect of dihydrostreptomycin, which enhances CM and depresses AP in the cat.[14] Selective depression of CM has been seen also in a viomycin-treated cat. In this animal the responses to pulsed tones show that a summating potential is still present.

In the guinea pig, kanamycin 400 mg/kg daily for 44 days produced complete loss of the Preyer reflex in response to sudden, intense sound. The cochlea of one of these animals shows a marked degenera-

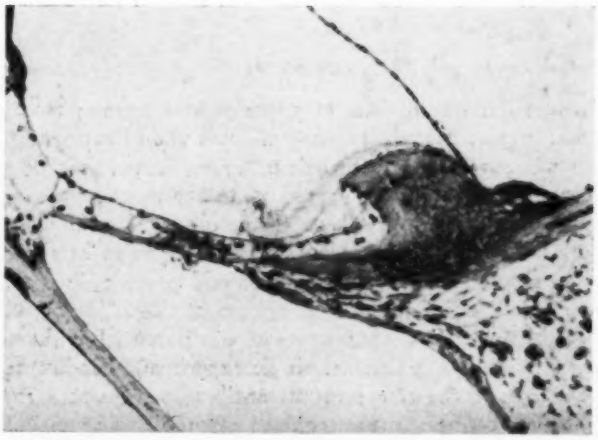

Fig. 11.—Rat 70, 2nd turn, kanamycin 750 mg/kg/day for 96 days. Loss of ganglion cells and nerve fibers.

tion of the organ of Corti which is greatest in the basal turn. In the upper turns, the nuclei of the internal hair cells are present, but only occasional nuclei of the external hair cells. The spiral ganglion presents a normal appearance, and the neuroepithelium of the crista is unaffected. Partial loss of Preyer reflexes has been seen in guinea pigs treated at 200 mg/kg. Microphonic measurements in guinea pigs are still to be made.

Rats seem to be less susceptible to kanamycin than either cats or guinea pigs. A reversible loss of response to the Galton whistle occurs in rats treated at 200 mg/kg daily, and a level of 400 mg/kg seems to be necessary to produce irreversible deafness. My associates, Mr. George Gourevitch and Mr. Martin Hack, who are psychologists skilled in the use of the operant techniques of the Skinner school, have been following the auditory thresholds of a few trained animals by a sort of Békésy audiometry that they have adapted to the rat after the manner of Blough and Ratliff, who studied dark adaptation in the pigeon.[15] Their results to date confirm the partial reversibility of the kanamycin effect in rats. Destruction of the auditory mechanism can occur, however, at higher dose levels, as seen in Fig. 11. This

photomicrograph shows the second turn of the cochlea of a rat treated with kanamycin 750 mg/kg daily for 96 days.

## COMMENT

Changes seen in the ears of experimental animals treated with kanamycin suggest that the primary effect is upon the organ of Corti. We cannot be sure whether the hair cells are affected first, or whether the changes seen in them are secondary to changes in the supporting cells. It is to be hoped that electron microscopic studies will furnish an answer to this question. The selective depression of the cochlear microphonic potential seen in the cat should provide, in conjunction with microscopic examination of the organ of Corti, further information as to the source and significance of this potential in the auditory process. Certainly it is the best single experimental indicator of the ototoxic effect of the streptomyces antibiotics. Further studies of the day-to-day changes in the cochlear potentials using an indwelling electrode on the round window after the manner of Vernier and Galambos[16] are needed.

## SUMMARY

In man, prolonged use of kanamycin in the therapy of tuberculosis has produced varying degrees of auditory impairment ranging from just detectable loss at 8000 cps to complete deafness, which occurred in two cases with pre-existing renal damage.

In cats kanamycin produced cochlear effects ranging from selective depression of the microphonic response to complete loss of all cochlear potentials. The organ of Corti appears to be the primary site of action of the antibiotic, but degeneration of the ganglion cells and nerve fibers can occur.

550 First Avenue

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The experiments on cats were done in the Merck Institute for Therapeutic Research, Rahway, N. J. The technical assistance of Walter J. O'Shanny is gratefully acknowledged.

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L

# FLUID EARS AND NERVE DEAFNESS

## CIRCA 1835

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(by invitation)

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In this era of rapid technological advance, many of us tend to become so engrossed in the changes, that we have little time to consider how our achievements are related to the advances of previous investigators. An occasional look backward is not wasted time. It is an opportunity to re-awaken a sense of humility when we see what others have accomplished with considerably less in the way of technical aids.

The recent reading of an otological magazine emphasized some of these ideas to us. This issue of the magazine, published in 1838 in book form, is a treatise on diseases of the ears by a German otologist, Dr. William Kramer.[1] The material therein is so sound and up-to-date that we deem it worthy of being shared. We have selected two short sections which have been edited only enough to delete obvious repetition, and to arrange some of the material in a more logical sequence. Other than our added comments, the text which follows was written in the early eighteen-thirties.

### INFLAMMATION OF THE MUCUS MEMBRANE OF THE MIDDLE EAR WITH ACCUMULATION OF MUCUS

#### INTRODUCTION

"In this form of disease, dullness of hearing occurs either unaccompanied by any painful sensation, or at most, merely by a feeling of fullness and weight in the ear, and even in the head; or with a sensation

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as though a veil or a flap were hung before the ear, which only required to be removed in order at once to restore the hearing. . . . One or both ears may be affected, and there may either be no singing in the ears or this may be present in all its most varied modifications. . . . Dullness of hearing is the only constant symptom of which all these patients complain, though this varies much in intensity. The disease may continue gradually to become worse, uninterrupted and unaffected by any changes of weather or similar influences; or it may continue unaltered for years, in the same state as that which it assumed at the onset.

### PATHOLOGY AND ETIOLOGY

"The similarity of structure between the mucous membrane lining the eustachian tube, and that of the mouth and nostrils; the simultaneous existence of catarrhal affections of these membranes; and the peculiar disposition which they all . . . [have] . . . to recur, place the inflammatory catarrhal character of the present disease beyond all doubt. From the same analogy, the entirely chronic character of the disease is manifest. [Though] it may last for years, nay, even during the whole life of the patient . . . it is and continues to be an accumulation of mucus; however long it may exist.

"Predisposition to mucous engorgement of the middle ear is most frequently seen in childhood and youth, where there is a disposition to mucous engorgements and catarrhal affections in general. [Can this be a reference to allergy?]

"Frequently only one ear is affected; but if both are, not only the dullness of hearing, but also the difficulty of overcoming the disease, is always greater in one ear than in the other.

"It is evidently of most frequent occurrence during moist autumns and springs, and in moist climates, e.g., in sea towns from which places the greater part of those patients have come to me. Under these circumstances, I cannot understand how the so-called English aurists, who must very frequently meet with the disease in a foggy city, like London, should have scarcely any notion of the proper diagnosis of the complaints, and still less of any rational mode of treatment. [No comment]

[Hypogammaglobulinemia was not mentioned as an etiological factor.]

### EXAMINATION AND DIAGNOSIS

"If the patient be more closely examined there is a constant or frequent stuffing of the head, [with] much secretion from the mouth and nose.

"The membrana tympani [is] shining, smooth, and transparent, notwithstanding great accumulation of mucus in the cavity of the tympanum.

[This is Dr. Kramer's sole comment on the examination of the drum. He states that all his examinations were made by direct sunlight. (It should be recalled that the head mirror would not be introduced by Von Tröltsch until 1855.) We submit that it is significant that Dr. Kramer does not mention seeing a fluid level line. For one who could see the drum only by direct vision the descriptive term "transparent" is certainly appropriate.]

Dr. Kramer adds, "No confidence therefore whatever ought to be placed in these [findings]. It is very different, however, with regard to the investigation of the eustachian tube itself.

[At this point Dr. Kramer advocates catheterization of the ear as the most important diagnostic procedure. About 100 years later, the present author stressed the importance of auscultation in the diagnosis of fluid in the ears and foolishly thought he was making an original contribution!]

### PROGNOSIS

"The prognosis is altogether favourable; even when the disease has been neglected, and has become firmly rooted, from having lasted for years, a complete cure, or a very material improvement, may be effected by submitting the patient to a proper plan of treatment. In quite recent cases, in which the mucous accumulation is very loose, more fluid in its nature, and rather confined to the eustachian tube, perhaps even simply to the mouth of the canal, nature [often] effects a cure. . . .

"In old cases, the favourable prognosis stated above, is often limited in a very annoying manner, from the great tendency there is to relapse. A radical cure is soonest and with most certainty effected, where the constitution of the patient is not generally disposed to mucous engorgement. [Certainly a reference to allergy.] When the throat, fauces, and nostrils are simultaneously suffering from considerable chronic catarrhal inflammation, the cure of the aural disease must not be reckoned till the surrounding mucous membranes are relieved of their disease; when, if the affection of the ear has been but recently established, it will sometimes vanish without any direct treatment of the middle ear.

TREATMENT

"As soon as the nature of the affection has been recognized, no time should be lost in having recourse to an appropriate general and topical plan of treatment. I shall, in the first place, speak of the *general treatment*, because when this is requisite, it *must always precede the topical.*

"Such food as tends to favour the secretion of mucus, e.g., beer, milk, butter, cheese, acids, etc., should be avoided. [What? No dust? It should be recalled that it will be nearly another hundred years before the word allergy appears in the medical literature.]

"When at the same time, there exists affections of the pharynx and nostrils, inflammatory redness of the fauces, pains about the throat frequently recurring, and swollen tonsils, it has been recommended to treat these.

[At this point Dr. Kramer gives reference to many of the then current therapeutic measures such as Russian vapor baths and the like. We shall omit mention of these and certain other local procedures, but wish to say that he cites two surgeons who suggested mastoidectomy as a possible cure. Kramer, reflecting the current opinion of his day, points out the grave danger to the life of the patient if this is done. (Wasn't it James Jervey, Sr., and Harold Tobey who first advocated mastoidectomy in our day?) He also suggests paracentesis of the drum followed by a water douche to force the fluid down the eustachian tube. He points out, however, that this can be accomplished only when the eustachian tube is open—never when it is closed to

traffic from the ear to the nasopharynx. There is nothing new under the sun, is there?]

"The only certain plan of procedure, in obstruction of the eustachian tube," Dr. Kramer adds, "is to act directly on its pharyngeal opening, and thus on the mucus accumulation.

### AUSCULTATION

[Dr. Kramer's description of auscultation sounds is made on the basis of ear to ear hearing. The auscultation tube was not yet a diagnostic tool, although it was soon to become popular after its introduction by Nicholas Deleau, a Frenchman.]

"The air-douche should, at first, always be allowed to act with only moderate force . . . to observe the impression which it makes on the diseased ear. . . . In the more favourable cases, a very distant noise is heard; namely, as a small portion of air enters the eustachian tube and acts on the plug of mucus, passing at first in small puffs, and at length in a fine stream to the membrana tympani. If the passage be still more free, the stream of air passes in a howling noise, which at length becomes converted into a rattling sound (resembling the fall of heavy rain on trees) when it obtains a completely free passage up to the membrana tympani. . . . The changes in the noise which the air makes on entering [the ear] afford the best rule for determining how long the operation should be continued, how often it should be repeated, and especially what should be the force of each douche. . . . If . . . no audible stream of air makes its way out into the tympanum the number of sittings should not exceed four and air douching should be abandoned.

"When both ears are affected, they should each be alternately submitted to the douche. After every douche that has passed through to the membrana tympani, a striking improvement of the hearing distance is observed. [This, Dr. Kramer measured with a watch. It is still about 20 years before tuning forks were in general use even though Weber published the principles of the test known by his name in 1835.] If the improvement continues for a few hours, or if it be not on the whole very considerable, the sittings should be continued daily; but if the improvement continues unaltered till the following day or longer, it is advisable not to make daily use of the douche. . . .

By waiting a few days or weeks even, we obtain the best tentatory preparation for the final termination of the treatment."

### CASE REPORT

CASE XL. "Mr. Ponath, of this place, forty years of age, of sound, spare constitution, after a severe cold, experienced a heavy dragging feeling on the right side of the head, with great dullness of hearing, and an incessant, loud buzzing in the right ear; the left continued perfectly sound. In vain had the patient endeavoured to render his ear again free, by twenty Russian vapour baths, and strong purgatives; he entirely failed. Three months had elapsed after these attempts when he consulted me. The heaviness in the head and tinnitus were still present; he heard my blowing through the catheter introduced in the right eustachian tube. I heard the air rush with a gurgling sound up to the membrana tympani, and there ensued immediately on this, an increase to twenty-four inches of the distance at which the watch could be heard. This simple inflation was repeated on the following day. The patient himself forced his breath into the cavity of the tympanum several times a day, and thus the gurgling noise, the tinnitus, the headache, and the difficulty of hearing diminished from day to day, and after eight days, were so completely lost, that the patient was dismissed as cured; so that it might be said of him that his disease, which had withstood several months' treatment by important remedies, had been BLOWN AWAY by a simple puff with the mouth."

### NERVE DEAFNESS

Here we will quote but one sentence interrupted by occasional comments.

"In this disease, a violent noise, especially a loud, screaming shrill voice, is insupportable [recruitment and uncomfortable loudness], or even painful to the ear [poor tolerance for loud sounds], and peculiarly unintelligible [over recruitment and poor discrimination score]; whilest a metallic, melodious, full-toned voice, moderately elevated [no shouting, please] and associated with distinct, slow utterance is agreeable to the ear, and easily understood." [Often better than with a hearing aid]

This sentence encompasses almost all of modern audiology. May we repeat it without the comments?

"In this disease, a violent noise, especially a loud, screaming shrill voice, is insupportable, or even painful to the ear, and peculiarly unintelligible; whilest a metallic, melodious, full-toned voice, moderately elevated, and associated with distinct, slow utterance is agreeable to the ear, and easily understood."

This statement was made about 125 years ago. Has it been said better since?

We submit, on the basis of these two bits of evidence, that Dr. William Kramer was an otologist, summa cum laude, circa 1835.

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LI

# ACOUSTIC TRAUMA FOLLOWING INTERMITTENT EXPOSURE TO TONES

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A subtitle for our paper might well be "Quantitative Studies of Acoustic Trauma." Today it is generally accepted that noise can and does produce hearing loss. The practical question is now, "How much exposure to noise is bad?" Three words in this question require definition before the question can be intelligently answered. These words are "bad," "noise," and "exposure."

In man we can most easily define "bad" in terms of how much threshold shift for tones at what frequencies and lasting for how long. "How long" is the dimension that distinguishes among permanent hearing losses, temporary threshold shifts, and lesser degrees of fatigue lasting only seconds or minutes. Systematic study of "badness" along the dimension of temporary threshold shift is being done by Ward, Glorig, Sklar and Summerfield.[1,2] For reasons that will be more apparent later in the paper we believe these studies to be of great practical importance. We cannot, however, study permanent hearing losses in man in this same systematic fashion. For these studies we must resort to experimental animals.

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From the Central Institute for the Deaf and Department of Otolaryngology, Washington University School of Medicine, St. Louis, Mo. Supported in part by Grant No. B-1710 from the National Institutes of Health.

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In experimental animals we have other dimensions for "badness" that we can use. The behavioral tests for threshold responses to tones as used in the cat by Neff,[3] by Schuknecht,[4] and by Miller[5] appear to be most closely comparable to the threshold audiograms obtained on man. After injury we can also measure the changes in bio-electric potentials produced in the cochlea and the VIII nerve and we can examine the cochlea for anatomical evidence of injury. In our studies we use these latter methods. We cannot specify the relations between hearing loss seen in the clinic or by behavioral studies and the anatomical injuries or the changes in bio-electric potentials, but we believe that these changes represent a convenient end-point or indicator for evaluating different exposures to noise.

"Noise" may be defined in terms of its level, its frequency spectrum and other measures such as the ratio of peak pressures in the noise to the average pressures. The "exposures" may be defined in terms of their overall duration and other temporal characteristics; e.g., steady noise, intermittent noise, etc. The dimensions we have used will be apparent as the specific experiments are discussed.

## BACKGROUND EXPERIMENTS

The background for our experiment with intermittent exposures is the set of experiments we reported at the International Conference on Audiology.[6] Here we attempted to equate different exposures to steady 500-cps tones of various levels and durations on the basis of threshold shift for the cochlear microphonic (CM) recorded from the third turn of the cochlea of the guinea pig and on the anatomical basis of the injuries produced. This method requires that some anatomic injury be clearly present so that we know that the exposure was actually injurious. Similarly the injury should be less than total destruction of the organ of Corti so that we will know that the exposure did not greatly exceed our threshold for anatomic injury. We have found that a threshold shift for the CM of about 40 to 60 db gives us useful grades of anatomic injury. Accordingly we use this method to monitor our exposures so that we do not have to wait for histological specimens.

We found that changes in threshold for the CM in the third turn of 40 to 60 db appeared when the products of the sound intensity and duration of the exposures to 500-cps tones were constant. An

exception occurred for the brief exposures above 135 db SPL. It appeared that these sound pressures could break the organ of Corti rather promptly and should be considered separately from the exposures at lower levels. The relation at the lower levels implied that the loss of CM response was related to the total acoustic energy in the traumatic stimulus.

The anatomical specimens did show that the exposures to higher sound pressures had produced more disruption of the organ of Corti than exposures at lower levels. Even neglecting the brief exposures, the equal-energy relation did not appear to predict injury quite so well as it had predicted loss of CM. When the energy level of an exposure was halved, somewhat more than twice the duration of exposure was required to produce an equivalent injury. The character of the injuries appeared to change as we used lower sound pressures for longer durations and we were not sure how to interpret the severity of the injuries in terms of their probable functional importance.

When we used the same method to evaluate exposures to a 300-600 cps band of noise, we found that for the same durations lower sound pressures for this octave band would produce the same injuries over a considerable range of exposures. The peak sound pressures of a noise may exceed the average sound pressure of the noise by substantial amounts. This finding supported the hypothesis that peak sound pressures as well as total sound energy made an important contribution to the injuries.

## INTERMITTENT EXPOSURE TO TONES

The study of acoustic trauma by exposure to intermittent sounds requires the introduction of several additional concepts. First we must consider the possibility of some recovery from an injurious process, during the periods when the sound is off. Ward et al[7] have demonstrated that even rather small rests from noise have an important bearing on the temporary threshold shifts observed in men. At some point we expect that the sums of exposures to noise given in divided doses will be less injurious than the same duration of exposure to noise given in a single dose.

The second concept we must consider is the duty cycle of the "on" and "off" periods of the sounds. The sound may be on any

amount between zero and 100% of the time. This allows for a great variety of intermittent sounds. Also we must consider how often the duty cycle is repeated. One practical limit is about 20 times a second. When a sound is turned on and off again this rapidly we experience the sensation of fusion and find it difficult to identify the separate "offs" and "ons." In effect the sound has become continuous but with a modulated intensity. At the other extreme is the sound that is presented once and is followed by an infinitely long period of off, i.e., the single traumatic exposure. The number of combinations of duty cycle and rates of cycling possible and of importance is clearly very great.

For our initial experiment we chose to use a 500-cps tone with a 28% duty cycle repeated 14 times a second. This was presented at levels of 133 db, 127 db, 123 db and 120 db for durations such that the sums of the "on" periods totaled 5, 40 and 80 minutes. Many decisions were required to make these choices. These decisions were based on prior experiments, on performance of immediately available equipment and on our estimate of the information we might expect in relation to an overall survey of trauma from intermittent exposures.

First it made sense to start near some probable limits with the intention of later working away from these limits. One limit we chose was that of insufficient time for recovery. Related to this limit was a rate of cycling that approached continuous noise. On this basis we repeated the on-off sequence 14 times a second. This sound does not fuse but the interruptions are too fast to count individually.

We had to have a duty cycle significantly less than 100% if we were to expect any differences from continuous sounds. On the other hand an acute experiment on an anesthetized guinea pig cannot go on much longer than six hours. Thus the duty cycle had to be rather more than zero percent. We found that our equipment would give us a duty cycle of 28% reliably when the rate of cycling was 14 times a second.

Our earliest experiments suggest two variables that would also need some control. First, the peak pressures of the band of noise appeared important to the injuries produced. By using a 500-cps tone instead of a noise for the "on" periods we could control the peak pressures. Secondly, the character of the injuries observed changed

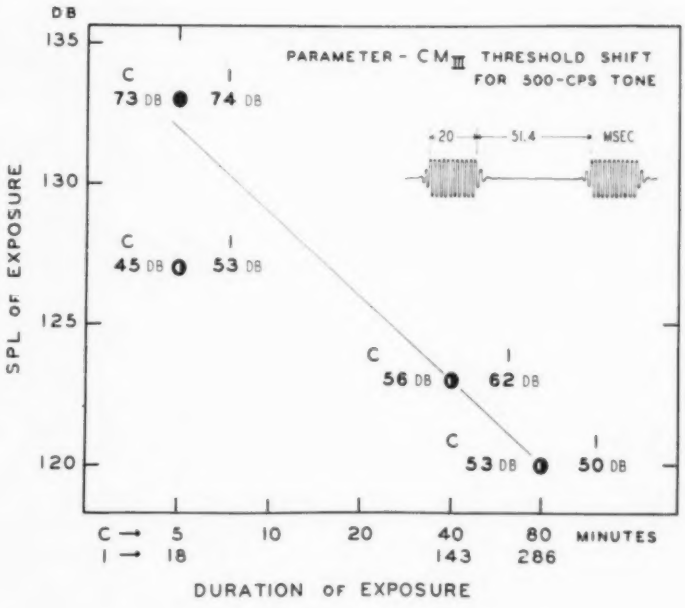


Fig. 1.—Acoustic trauma in the guinea pig produced by intermittent and continuous 500-cps tones. Each point describes the SPL and duration of two sets of exposures, one continuous and one intermittent. The numbers indicate the median shifts in 3 microvolt threshold for CM recorded from the third turn of the cochlea. The dimensions of the intermittent stimuli were as shown. The line is drawn so as to connect exposures of equal acoustic energy.

somewhat in the progression from brief exposures with high sound pressures to the longer exposures with lower sound pressures. To control for this we chose corresponding and representative combinations of exposure to the intermittent tones. In other respects the methods and instrumentation used were the same as reported in earlier studies.[6,8]

The exposure combinations and the results are shown in Figure 1 for both the intermittent exposures and a parallel set of continuous exposures. Each point represents five to eight ears exposed to each

condition. The total durations of the intermittent exposures are plotted so that the sums of their "on" periods correspond to the exposures to continuous tones. The numbers denoted by "C" and "I" correspond to the median threshold shifts in the CM response of the third turn of the cochlea to a 500-cps test tone. In most cases the mean values were the same. None of the differences shown were statistically significant. The light line is drawn to show combinations of duration and sound pressure for exposures that have equal energy. It is located one decibel below the line drawn for the earlier study[6] and appears to be a reasonable duplication of the previous findings.

The anatomical injuries found in the third turns of these cochleas were the same for each set of intermittent and continuous exposures. The tendency for the character of injury to change at lower pressures and longer durations also appeared. The details of these anatomical changes are the same as those reported for the earlier study.

From our findings we can conclude that both loss of CM and injury to the organ of Corti were related to the "on" fraction of the intermittent stimuli used in the experiments. In spite of the relatively obvious nature of this conclusion three statements about the processes of injury and recovery from injury are now possible. First, injury was confined to the "on" fractions of the exposure and did not accrue during the "off" periods. Second, recovery did not occur during the "off" periods. Third, the first two statements are independent of sound pressure and duration for the range of exposures used. These statements clarify the relations to be studied in the future and lead immediately to three specific questions: 1) "Will a smaller duty cycle, e.g., 5%, allow recovery processes to appear?" 2) "How long must we make the 'off' period of the duty cycle before we see evidences of recovery?" This involves a change in both duty cycle and rate of repetition. 3) "How much sound can we put in the 'off' period without increasing the injuries produced?"

The practical usefulness of this finding is less certain at the moment. This is because of the way sound level meters average intermittent sounds. This particular intermittent sound was approximately 5.5 db less injurious than the continuous sound. One standard sound level meter showed, with both fast and slow meter settings, that the intermittent sound was about 3 db less than the continuous sound. Thus the meter over-rated the potential for injury by 2.5 db. We

cannot, however, generalize further except to note that for a variety of intermittent sounds sound level meters can give readings that may be somewhat high, correct, or low with respect to the potential for injury.

## SPECIES DIFFERENCES

Recently we have been made more acutely aware of another limitation on the direct practical application of results from these studies. Enough comparable studies are now under way on the cat and the guinea pig to suggest that there may well be important species differences that are qualitative as well as quantitative. Last year Lawrence[9] reported striking hysteresis and injury phenomena for the CM recorded from the cochlea of the cat at sound pressures as low as 114 db. In a preliminary report to the U.S. Air Force, Miller[5] has found permanent threshold shifts of 30 to 60 db by behavioral tests on the cat after a two-hour exposure to "white" noise at 115 db. These losses were much greater than either we or Miller would have expected. The earlier studies of Hawkins, Lurie, and Davis[10] suggested that the unanesthetized cat was resistant to acoustic trauma. However, Miller's findings agree rather well with a prediction based on Lawrence's findings.

In the guinea pig we routinely measure the cochlear potentials with brief bursts of tones up to 120 db and do not see the hysteresis in CM that Lawrence reports in the cat. Even when we use longer bursts (4 sec.) of a 1000 cps tone so as to correspond more closely to the conditions reported by Lawrence, the hysteresis and loss of CM response do not appear until the sound pressure level is raised to 130 or 135 db. At these higher levels the results for the guinea pig become qualitatively the same as those reported by Lawrence for the cat.

Similarly we would not predict from our experience that the guinea pig would show large losses of CM after the exposures Miller used for the cat. We tried the same exposures on several guinea pigs. Characteristic results are shown in Figure 2 for the potentials recorded from the first turn of the cochlea. The three panels show the control potentials, the potentials recorded one hour after exposure, and the potentials recorded 13 days after exposure.

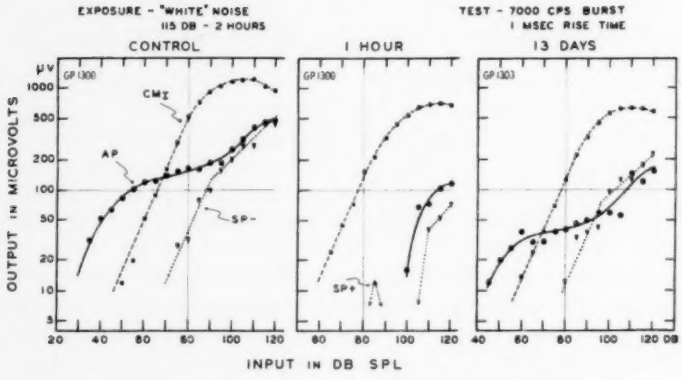


Fig. 2.—Input-output functions for potentials recorded from the basal turn of the cochlea of the guinea pig after acoustic trauma by "white" noise. $CM_1$, cochlear microphonic of basal turn; AP, nerve action potential; SP–, negative summating potential; SP+, positive summating potential.

The control potentials and the potentials one hour after exposure were recorded from the same ear. The potentials recorded 13 days after exposure were obtained from another ear. The latter guinea pig was anesthetized as usual for the exposure but the bulla was not opened for insertion of cochlear electrodes. Thirteen days later the guinea pig was again anesthetized and the electrodes inserted as usual. Replications of these experiments show the variations in response to be small when we use a "white" noise for the exposures. In each panel are shown the input-output functions for CM, nerve action potential (AP) and summating potential (SP) for a 7000 cps tone burst. The CM response is only 11 db less sensitive one hour after exposure and shows little change subsequently. The CM responses recorded from the third turns of these cochleas showed comparable small changes. The most striking change appears in the AP responses. One hour after exposure the 10 microvolt response has shifted 66 db and the response at 120 db has decreased from 460 microvolts to 118 microvolts. Thirteen days after exposure the 10 microvolt response is shifted only 13 db but the response at 120 db is still only 150 microvolts. The AP responses to 500-cps bursts show comparable changes.

Most of the AP recorded by our electrodes arises from the neural elements of the basal turn of the cochlea. More severe acoustic trauma, as judged by changes in CM responses, with 500-cps tones and with the 300-600-cps band of noise often produced less change in the maximum output of the AP responses. The AP function 13 days after exposure suggests that only one-third of the neurons are capable of a response, but some of these clearly can respond at levels little different from the normal threshold. We would not predict threshold shifts of 30 - 60 db as observed in the cat. We are not sure yet how to interpret these findings in terms of practical hearing loss.

## COMMENT

Since there appear to be differences in sensitivity to acoustic trauma between the guinea pig and the cat, we must remain alert for similar differences between man and experimental animals. Relating experiments involving permanent injuries in animals to experiments using temporary threshold shift (T.T.S.) in man can lead to difficulties of interpretation. Ward et al[2] found for man that T.T.S. has a relation to intensity and duration of exposure that is different from the relation shown for acoustic trauma in the guinea pig. For some exposures both sets of data agree that exposures of equal total energy give equal T.T.S. and equal loss of CM, but fundamental differences remain. For intermittent exposures the loss of CM is proportional to the "on-fraction" multiplied by the duration of exposure whereas T.T.S. is proportional to the "on-fraction" multiplied by the logarithm of the duration of exposure. Also results of the animal experiments clearly indicate that the equal-energy relation reaches a limiting sound pressure at which loss of CM and cochlear injury depend more strongly on the sound pressure than on the duration of the exposure. The relations established by Ward et al for man suggest instead that, for brief exposures, higher sound pressures than those predicted by an equal-energy relation are required to maintain a constant T.T.S. Until we understand the nature of these differences practical application of the results of the animal experiments can only be speculative.

## SUMMARY

In earlier experiments it was shown that exposures to 500-cps tones produced constant loss of CM when the acoustic energy of the exposures was constant. This relation obtained for exposures ranging

from 133 db SPL for five minutes to 118 db SPL for 160 minutes. In a new series of experiments intermittent 500-cps tones with a 28% duty cycle and a rate of repetition of 14 bursts per second produced losses of CM and cochlear injuries indistinguishable from those produced by continuous exposures when the sum of the "on" periods equalled the continuous periods. The conclusions of the earlier experiment were confirmed and can be enlarged to include intermittent bursts of tone by describing effective duration of exposure in terms of the "on" fractions of the tones. The application of these results to man is limited by species differences and by lack of knowledge of the relations between cochlear injury in animals and temporary threshold shift in man.

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LII

# AN EXPERIMENTAL STUDY OF THE DYNAMIC CIRCULATION OF THE LABYRINTHINE FLUIDS

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In a previous publication[1] it has been suggested that the circulation of the labyrinthine fluids is probably a dynamic process. This paper reports experiments with dyes as the second of a series of various methods of investigation to determine the origin and absorption of the labyrinthine fluids in living animals. Fluorescein (molecular weight 332.296) and trypan blue (molecular weight 960.808) were selected. This approach was tried because it is simple and the advantages and disadvantages of these dyes are well known. It was realized that the use of dyes alone could never provide all the information required. It was hoped, however, that this method might supply sufficient data to provide a foundation for research of a more complex nature.

Guild[2] used Prussian blue to investigate the circulation of endolymph and Altmann and Waltner[3] examined both endolymph and

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perilymph with the same dye. Ventura-Gregorini,[4] Gisselson,[5] Graf and Poretti,[6] and Kley[7] employed fluorescein to determine the origin of labyrinthine fluids. Among others, Lurie[8] noted that trypan blue did not enter the labyrinthine fluids when injected in safe doses intravenously.

## METHODS

In these experiments, over 200 guinea pigs weighing 250 to 350 grams, two adult cats, and two rabbits weighing 1 to 2 kilograms were used. All animals were rendered insensible to pain with parenteral sodium pentobarbital (40-50 mg per kilogram) and the local infiltration of 2% procaine with epinephrine 1-50,000.

Exposure of various parts of the inner ear required two surgical approaches: 1) through the external auditory canal, and 2) through the bulla. The round window and oval window could be observed after minor surgery which involved only slight trauma. A small incision three to four mm was made in the skin and cartilage of the auricle between the tragus and antitragus. Then with the aid of a Zeiss operating otoscope (6X to 40X) the external auditory canal and tympanic membrane were studied. The external auditory canal was cleared of cerumen and foreign bodies. If the tympanic membrane were not transparent, infection of the middle ear was suspected, and if pus were present the experiment was abandoned. In healthy animals a Fowler pick was used to perforate the tympanic membrane (posterior superior aspect). Proper rotation of the head permitted a full view of the round window. Additional manipulation of the head allowed adequate visualization of the incudostapedial joint, the stapes, and its footplate.

Observation of the cochlea and exposure of the spiral ligament by a fenestra were done according to methods described by Weille et al.[9] The inferior cochlear vein was made accessible according to the description of Perlman.[10]

The dyes used were trypan blue 5% or 10% and fluorescein 3%, 10%, or 20%. In some experiments, 0.05 ml to 2 ml of these dyes were injected approximately in 10 seconds into the spinal fluid at the lumbar area. In other experiments, 0.5 ml to 2.5 ml were given intravenously. Various areas of the inner ear were observed with mi-

croscopes during and after these injections. In all experiments detection of the dye depended entirely on visual criteria.

## EXPERIMENTS

*Intraspinal.* While the round window membrane was observed microscopically (25X with blue filter), 3%, 10%, or 20% fluorescein 0.05 ml to 2 ml were injected into the spinal fluid of living guinea pigs at the lumbar area. In these preliminary experiments, dye was seen pouring out of the labyrinthine opening of the cochlear aqueduct to stain the membrane of the round window within seconds. Twenty guinea pigs then were injected similarly with 0.2 ml of 3% fluorescein and observed. At the round window the fluorescein appeared within 2 to 18 seconds. In five other guinea pigs, 0.05 ml of 3% fluorescein intraspinally was noted at the round window within 30 seconds. In one cat 2.1 ml of 10% fluorescein was given into the spinal fluid at the lumbar area. Within 6.5 minutes the round window membrane was stained. One rabbit was treated similarly to the cat (0.5 ml of 10% fluorescein). The membrane of the round window of this rabbit showed stain within two minutes.

Two guinea pigs received 0.2 ml of 5% trypan blue into spinal fluid at the lumbar area. Within ten seconds the membrane of the round window was stained.

Twenty-four guinea pigs treated intraspinally with 0.2 ml of 3% fluorescein showed the dye at the round window within a few seconds. Sixteen were kept alive for 24 hours, four for 48 hours, and four for 72 hours. In only four animals was there any evidence of dye at the round window within 24 hours. One of these four animals did poorly after the injection and his round window membrane was deeply stained after 24 hours. Incidentally, this animal died shortly after the 24-hour observation. The other three animals showed no dye at the round window after 48 and 72 hours.

In two guinea pigs a mixture (0.05 ml of fluorescein 3% and 0.15 ml of a 1-10 dilution of Higgins' India ink) was injected intraspinally at the lumbar vertebral area. As usual, the fluorescein appeared at the round window within seconds and cleared within 24 hours, but no India ink appeared until 48 hours, and after 72 hours the amount of India ink increased.

The cochlea was exposed in twenty guinea pigs, and 0.2 ml of 3% fluorescein was injected intraspinally. The basal turn stained within seconds, but at the end of two hours only the first three turns showed staining. The first was always stained more deeply than the third turn. When a fenestra was made at the apical turn or the stapes was removed and perilymph allowed to escape, the whole cochlea was quickly stained. Five other guinea pigs were killed two hours after the intraspinal injection of fluorescein and kept at 4° C. for twenty-four hours. At this time the whole cochlea was stained.

When a fenestra was made in 37 guinea pigs on the second or third turn of the cochlea to expose the spiral ligament over the scala vestibuli, the scala media, and the scala tympani, and 0.2 ml of 3% fluorescein was placed into the spinal fluid at the area of the lumbar vertebrae, the spiral ligament was stained over all three scalae within 20 to 80 seconds.

Four guinea pigs were killed, and 0.2 ml of 3% fluorescein was given intraspinally. The membrane of the round window was stained within six seconds.

The inferior cochlea vein was exposed in two guinea pigs, and the wall of the vein was pierced. A small bone wax plug was inserted into the area where bone was removed to expose the vein. Then 0.2 ml of 3% fluorescein was given intraspinally. Within a few minutes the wax plug was removed and the blood which issued from the hole appeared stained.

*Intravenous.* The round window and cochlea of eight guinea pigs were observed during and following the intravascular injection of 0.2 ml to 0.5 ml of 3% fluorescein. In three of these animals the spiral ligament was exposed by means of a fenestra. The observed areas appeared stained within 6 to 90 minutes. In the guinea pig it was difficult to ascertain if all of the dye was injected intravascularly. Twenty-seven guinea pigs, therefore, were given 1 ml of 20% fluorescein subcutaneously, and observed areas were stained within two hours. Two of these animals injected subcutaneously were kept alive 24 hours, and in both the dye had disappeared from the inner ear at that time.

One cat and one rabbit were prepared so that the round window was under observation. The cat received 2.5 ml of 20% fluorescein

intravenously and the rabbit 1 ml of 20% fluorescein intravenously. In the cat the round window membrane was stained within six minutes, and in the rabbit the round window membrane showed the dye within six minutes.

The cochlea and round window in two different guinea pigs were observed for about 60 minutes after the intravenous injection of 0.5 ml of 5% trypan blue. Skin, footpads, mucosa of nose, and the bulla were deeply stained, but the cochlea and round window showed no stain. In ten others, 1 ml of 10% trypan blue was given subcutaneously in the axillary region. No dye was noted at the round window or the cochlea after 1, 2, 4, 24, and 48 hours. On dissection at the end of 48 hours, the membranous labyrinth near the stria vascularis was stained. Animals dissected previous to 24 hours showed no such staining.

## COMMENT

These experiments with living animals suggest three possibilities: 1, the circulation of the labyrinthine fluids is dynamic; 2, the labyrinthine fluids may be derived from at least two sources (blood and spinal fluid); and 3, various constituents of the labyrinthine fluids may arise from different origins.

The first possibility is supported by the data which showed that fluorescein in the inner ear of living guinea pigs always cleared within 48 hours. When guinea pigs were killed just after staining with fluorescein, the dye never left the inner ear.

The second possibility is supported by the fluorescein experiments in guinea pigs, cats, and rabbits. When the dye was injected intraspinally or into the systemic circulation, this foreign substance, fluorescein, appeared promptly in the inner ear. These data suggest that perilymph and endolymph may be derived from both the blood and cerebrospinal fluid. When the spiral ligament over the scala media, scala tympani, and scala vestibuli was observed after the intravenous or intraspinal injection of fluorescein, staining was found over all scalae. From these data one might infer that both endolymph and perilymph may originate from blood or cerebrospinal fluid. The fact that intravenous fluorescein stained the whole cochlea whereas this dye when given intraspinally stained only part of the cochlea adds support to this second possibility.

The third possibility rests on the trypan blue and India ink experiments. When a mixture of India ink and fluorescein was placed in the cerebrospinal fluid, the fluorescein appeared and disappeared from inner ear fluids before India ink was even noted. In addition, the India ink was not cleared from the inner ear. These data point to a difference between large and small molecules in movement into and absorption from the labyrinthine fluids. Trypan blue (molecular weight 960.808) appeared in the cochlea via the cerebrospinal fluid, but did not appear in the cochlea on the intravenous injection. Fluorescein (molecular weight 332.296) readily entered the cochlea from either the systemic circulation or the cerebrospinal fluid. All such data imply that various constituents of labyrinthine fluids may come from different sources.

The advantages of the described experiments include the use of living animals and observations made during and after the injection of dyes. Much is left to be desired, however, as the testing agents are not normal constituents of the body and therefore may have toxic effects on normal metabolic processes.

## CONCLUSION

Experiments with fluorescein and trypan blue in guinea pigs and other animals indicate that the circulation of the labyrinthine fluids is a dynamic process.

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LIII

# LONG TERM RESULTS OF SURGERY FOR OTOSCLEROTIC DEAFNESS

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When Julius Lempert[1] published his results of the fenestration operation for otosclerosis they were received with hope by a few but with considerable skepticism by many. It was the opinion of most that although the deafness of otosclerosis might be improved by his operation the improvement would probably be only temporary: 1) because the disease was not being treated, 2) because the fenestra would probably close and 3) because of the expectancy of further nerve degeneration so frequent in otosclerosis.

In the twenty years that have elapsed since his first report the hope of the few has been realized, the doubt of the many dispelled. There is no longer any question that the deafness of otosclerosis can be improved by a fenestration and that the results are lasting.

Rosen[2] revived Miot's operation for mobilization of the stapes and published his results of two years experience in 1955. He reported fourteen cases successfully mobilized that had maintained serviceable hearing for the two years. He did not state in that paper how many cases had been attempted.

It is my purpose in this presentation to report the results of all our cases of fenestration and of mobilization in order to compare the immediate and long term results of the two procedures and to compare their relative efficacy in relieving the deafness of otosclerosis.

## FENESTRATION

In a recent paper[3] we published the results in 818 consecutive patients fenestrated for otosclerosis. Of the 818 cases 658 were avail-

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able for study. Of the 160 not included 132 had had a cartilage stopple used and were therefore not counted, 2 had no speech audiometry performed (they were foreigners and not suitable for testing with English speech), 12 were lost to postoperative follow-up and 14 were fenestrations after unsuccessful attempted stapes mobilization and are reported elsewhere.[4] Table I shows the immediate (1 to 3 months) postoperative levels of hearing for speech in these cases.

TABLE I

DISBRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL FOR SPEECH (SPONDEES) ONE - THREE MONTHS AFTER OPERATION

| HEARING LEVEL (db) | FENESTRATION | | |
|---|---|---|---|
| | No. | Percent | Cumulative |
| 20 db or better | 98 | 14.8 | |
| 21-25 | 191 | 29.1 | 43.9 |
| 26-30 | 170 | 25.8 | 69.7 |
| 31-35 | 84 | 12.8 | 82.5 |
| 36-40 | 44 | 6.7 | 89.2 |
| 41 db or worse | 71 | 10.8 | |
| | 658 | 100.0 | |

(Cases 1 - 818)

In order further to evaluate the results in terms of experience and of changes in technique these cases were broken down into three chronological groups. Group I 199 cases were operated upon from January 1945 to July 1949, Group II 232 cases from September 1949 to May 1953 and Group III 227 cases from May 1953 to July 1956. Table II shows these results and it is apparent that experience and changes in technique have improved the results considerably.

Of the initially successful cases closure of the fenestra occurred in 14.9% of Group I, in 2.8% of Group II and 3.3% of Group III. The closure rate therefore for the last 459 cases is approximately 3%. In all cases the closure of the fenestra occurred in less than one year after operation.

TABLE II

PERCENTAGE AND CUMULATIVE PERCENTAGES OF EACH GROUP HAVING THE INDICATED POST-OPERATIVE (3 MONTHS) HEARING LEVEL FOR SPONDAIC WORDS

| Hearing Level (db) | GROUP I | | | GROUP II | | | GROUP III | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Percent | Cumulative Percent | N | Percent | Cumulative Percent | N | Percent | Cumulative Percent |
| 20 db or Better | 6 | 3.0 | | 28 | 12.1 | | 64 | 28.2 | |
| 21-25 | 49 | 24.6 | 27.6 | 68 | 29.3 | 41.4 | 77 | 32.6 | 60.8 |
| 26-30 | 61 | 30.7 | 58.3 | 68 | 29.3 | 70.7 | 41 | 18.1 | 78.9 |
| 31-35 | 28 | 14.1 | 72.4 | 29 | 12.5 | 83.2 | 27 | 11.9 | 90.8 |
| 36-40 | 20 | 10.0 | 82.4 | 15 | 6.5 | 89.7 | 9 | 4.0 | 94.8 |
| 40 db or Worse | 35 | 17.6 | | 24 | 10.3 | | 12 | 5.2 | |

## LONG TERM RESULTS

We could follow with complete hearing studies 406 cases whose hearing level at the end of one year after operation was 35 decibels or less and who had had tests at two years or more after operation. Of these 406 cases there was no change in the hearing or less than 5 decibels change in 352 or 86.7%. There was a loss of 5 decibels or more from the hearing level at one year in 54 or 13.3%. Thirty-six of the 54 cases had lost between 5 and 8 decibels of hearing for speech at their last postoperative test and this is within the limit of random fluctuations in the hearing. One could expect the same patients to improve by the same amount at subsequent tests. This has been pointed out in the statistical analysis recently from these same cases.[3] In only 18 patients (4.4%) does the hearing appear appreciably worse as a result of the lapse of time, and these changes too are within the limits of random fluctuation.[5]

## STAPES MOBILIZATION

There have been 312 operations for mobilization of the stapes from November 1954 until December 1958. The hearing levels for speech, 1 to 3 months after operation in these cases, are shown in Table III.

TABLE III

DISTRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL FOR SPEECH (SPONDEES) ONE - THREE MONTHS AFTER OPERATION

| HEARING LEVEL (db) | STAPES MOBILIZATION | | |
|---|---|---|---|
| | No. | Percent | Cumulative Percent |
| 20 db or better | 66 | 21.2 | |
| 21-25 | 25 | 8.0 | 29.2 |
| 26-30 | 30 | 9.6 | 38.8 |
| 31-35 | 27 | 8.7 | 47.5 |
| 36-40 | 31 | 9.9 | 57.4 |
| 41 db or worse | 133 | 42.6 | |
| | 312 | 100.0 | |

(Cases 1 - 323)

Again in order to evaluate the effect of experience and changing of techniques the cases were broken down into chronological groups, Group I operated upon from November 1954 to December 1956 (118 cases) and Group II from January 1957 to December 1958 (194 cases). The results are shown in Table IV. Just as in the case of fenestration it is seen that the results of mobilization improve with experience. It is interesting to compare these immediate postoperative results of the two operations and such a comparison is seen in Table V for the total number of cases in both groups and more specifically in Table VI for the most recent cases in both groups.

It is interesting here to note that in spite of the theoretical possibility of reaching the nearly zero level of hearing for speech with an intact ossicular chain as is present in the mobilization procedure and on the contrary the theoretic optimum of a 20 decibel level for speech following fenestration actually 4% more of fenestration cases reach better than 20 decibels for speech than do mobilizations. The number restored to really serviceable hearing (30 db or better) by the two procedures is even more striking, 45.3% against 78.9%.

TABLE IV

DISTRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL FOR SPEECH (SPONDEES) ONE - THREE MONTHS AFTER OPERATION

STAPES MOBILIZATION

| HEARING LEVEL (db) | GROUP I | | | GROUP II | | |
|---|---|---|---|---|---|---|
| | No. | Percent | Cumulative Percent | No. | Percent | Cumulative Percent |
| 20 db or better | 19 | 16.1 | | 47 | 24.2 | |
| 21-25 | 7 | 5.9 | 22.0 | 18 | 9.3 | 33.5 |
| 26-30 | 7 | 5.9 | 27.9 | 33 | 11.8 | 45.3 |
| 31-35 | 9 | 7.6 | 35.5 | 18 | 9.3 | 54.6 |
| 36-40 | 12 | 10.2 | 45.7 | 19 | 9.8 | 64.4 |
| 41 db or worse | 64 | 54.3 | | 69 | 35.6 | |
| | 118 | 100.0 | | 194 | 100.0 | |
| | (Cases 1 - 124, November 1954 to December 1956) | | | (Cases 125 - 323, January 1957 to December 1958) | | |

Insufficient time has elapsed to permit exact comparison of long term results. Nor is there a sufficient number of cases of mobilization to be exactly comparable. Of the 148 cases of mobilization with a hearing level of 35 decibels or less 1 to 3 months after surgery we have complete hearing tests on 69 at one or more years after operation. Fifty-six of the 148 are too recent to have had a test at one year after surgery and for the 23 long term data are not available. Of the 69 cases we have had tests one or more years after operation as follows:

| | |
|---|---|
| 4 years | 4 cases |
| 3 years | 8 cases |
| 2 years | 30 cases |
| 1 year | 27 cases |
| | 69 |

Of these one is a failure because the improvement from operation was only 8 decibels. All the rest (68) are considered successes as all had more than 11 decibels gain and reached 35 decibel level or better. Of

TABLE V

DISTRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL FOR SPEECH (SPONDEES) ONE - THREE MONTHS AFTER OPERATION

| HEARING LEVEL (db) | STAPES MOBILIZATION | | | FENESTRATION | | |
|---|---|---|---|---|---|---|
| | No. | Percent | Cumulative Percent | No. | Percent | Cumulative Percent |
| 20 db or better | 66 | 21.2 | | 98 | 14.8 | |
| 21-25 | 25 | 8.0 | 29.2 | 191 | 29.1 | 43.9 |
| 26-30 | 30 | 9.6 | 38.8 | 170 | 25.8 | 69.7 |
| 31-35 | 27 | 8.7 | 47.5 | 84 | 12.8 | 82.5 |
| 36-40 | 31 | 9.9 | 57.4 | 44 | 6.7 | 89.2 |
| 41 db or worse | 133 | 42.6 | | 71 | 10.8 | |
| | 312 | 100.0 | | 658 | 100.0 | |
| | | (Cases 1 - 323) | | | (Cases 1 - 818) | |

these 68 cases 11 have reverted to approximately the pre-operative level and can be considered analogous to closures (16.2%). Eleven additional cases have lost 8 to 16 decibels of their original gain; of these, however, 9 still show a hearing level of 35 decibels or better at one, two or three years. The remaining 2, although they have a hearing level of more than 35 decibels are still much improved over the pre-operative level (16 decibel gain remains in each and they have hearing levels of 47 and 36 decibels). Whether these 11 will continue to lose more hearing remains to be seen. With two exceptions the remaining 46 cases or 67.6% show no appreciable change.

The two exceptions are interesting. One with an initial postoperative hearing level of 27 decibels shows an additional gain of 19 decibels after four years and now has a hearing level of 8 db for speech. The other had an initial postoperative hearing level of 28 decibels and shows an additional gain of 16 decibels after two years and has a hearing level now of 12 decibels.

## COMMENT

In this survey we have reported the results of fenestrations and mobilizations in terms of hearing levels for speech. We use speech

TABLE VI

DISTRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL FOR SPEECH (SPONDEES) ONE - THREE MONTHS AFTER OPERATION

| HEARING LEVEL (db) | MOST RECENT CASES | | | | | |
|---|---|---|---|---|---|---|
| | STAPES MOBILIZATION | | | FENESTRATION | | |
| | No. | Percent | Cumulative Percent | No. | Percent | Cumulative Percent |
| 20 db or better | 47 | 24.2 | | 64 | 28.2 | |
| 21-25 | 18 | 9.3 | 33.5 | 74 | 32.6 | 60.8 |
| 26-30 | 23 | 11.8 | 45.3 | 41 | 18.1 | 78.9 |
| 31-35 | 18 | 9.3 | 54.6 | 27 | 11.9 | 90.8 |
| 36-40 | 19 | 9.8 | 64.4 | 9 | 3.9 | 94.7 |
| 41 db or worse | 69 | 35.6 | | 12 | 5.3 | |
| | 194 | 100.0 | | 227 | 100.0 | |
| | (Cases 125 - 323) | | | (Cases 568 - 818) | | |

as the signal rather than averaging the pure tones at 500, 1000 and 2000 cycles because we find the test is faster to do, repeatable and is as nearly objective as any test of hearing can be. I agree that averaging the pure tones through the speech frequencies gives a comparable level and to test this we tabulated the results in 259 mobilizations on whom we had pure tone tests at the same time by the same audiometrist who did the speech tests. Table VII shows the comparative results and it is seen that when results are calculated in reference to pure tones they are a little bit better than when speech is used.

Lempert established the criterion of the 30 decibel level as serviceable hearing. He based this on pure tones through the speech frequencies. This is a good criterion and should stand. I would point out, however, that anyone who has a 35 decibel hearing level for speech with good discrimination is socially adequate. It is interesting to note also that in our mobilization results the same percent of patients reach the 35 decibel level for speech as those who reach the 30 decibel when tested by pure tones. We feel, therefore, that it is reasonable to consider a hearing level of 35 decibels tested with speech as serviceable hearing and as a good result.

TABLE VII

DISTRIBUTION OF CASES AS A FUNCTION OF HEARING LEVEL ONE - THREE MONTHS AFTER STAPES MOBILIZATION, COMPARISON OF LEVEL FOR PURE TONES (AVERAGE OF 500, 1000, 2000) AND LEVEL FOR SPEECH (SPONDEES).

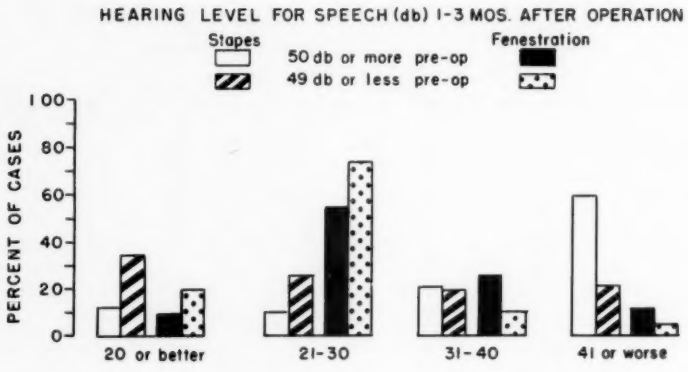
| HEARING LEVEL (db) | SPEECH | | | PURE TONES | | |
|---|---|---|---|---|---|---|
| | No. | Percent | Cumulative Percent | No. | Percent | Cumulative Percent |
| 20 db or better | 66 | 21.2 | | 60 | 23.1 | |
| 21-25 | 25 | 8.0 | 29.2 | 28 | 10.9 | 34.0 |
| 26-30 | 30 | 9.6 | 38.8 | 35 | 13.5 | 47.5 |
| 31-35 | 27 | 8.7 | 47.5 | 26 | 10.1 | 57.6 |
| 36-40 | 31 | 9.9 | 57.4 | 15 | 5.8 | 63.4 |
| 41 db or worse | 133 | 42.6 | | 95 | 36.6 | |
| | 312 | 100.0 | | 259 | 100.0 | |
| | | (Cases 1 - 323) | | | (Cases 1 - 323) | |

In comparing the two procedures it is quite obvious that from the point of view of economy both in time off from work and in hospital expense mobilization is preferable to fenestration. Furthermore, after mobilization, barring the accident of a permanently perforated tympanic membrane, the patient has a normal ear and has no restriction of activity. After fenestration, on the other hand, the patient has a cavity which needs care at intervals for the rest of his life. Nevertheless when good hearing is the required result there is no doubt but that fenestration is the operation which should be advised. This is particularly true in those patients with binaural hearing levels of 50 decibels or more.

It has been said that when mobilization fails fenestration can always be done subsequently. In general this is true and the result in 58 cases of fenestration after unsuccessful mobilization are quite comparable to those in which a fenestration was done initially.

There are many patients suitable for mobilization on whom one would not advise fenestration. For example, the person with a 45 decibel loss in one ear and nearly normal hearing in the other. In such a case mobilization is surely worth while providing the patient really understands the chances of success and failure and is aware that

TABLE VIII




complete loss of hearing in the operated ear is not an impossibility. Whether the other type of case which one might call the "long shot," for example, a patient with more than 70 decibels loss for speech or a 60% or worse discrimination score, should be operated on is an interesting question. We have done mobilizations in 42 such cases. In 10 of them (23.8%) the result would be considered successful. The postoperative hearing levels in these 10 cases were 21, 25, 32, 34, 28, 4, 40, 20, 44 and 44. In 9 of the 32 unsuccessful cases, however, fenestration was subsequently done and the thresholds post fenestration in these cases were 24, 21, 41, 18, 47, 29, 30, 43 and 44.

In predicting the results of any operation one can only refer to his own experience. To a patient with otosclerotic deafness one can say that he has 79 chances out of 100 of attaining a 30 decibel level for speech and 91 chances out of 100 for having a hearing level for speech of 35 decibels or better from the fenestration operation. With mobilization his chance of attaining a 30 decibel level is 45 out of 100 and of attaining a 35 decibel level or better 55 out of 100. If one wishes to be more specific one can take the pre-operative hearing level and predict that in a case with a pre-operative hearing level of 49 decibels or less 34 out of 100 will attain a hearing level of better than 20 decibels while 59 out of 100 will have a level better than 30

decibels from mobilization. In the same category 19 out of 100 will attain a better than 20 decibel level from fenestration and 86 out of 100 will have a hearing level of better than 30 decibels from fenestration. If the initial hearing is 50 decibels or worse mobilization offers 12 chances in 100 of a final hearing of better than 20 decibels and 21 in 100 of hearing better than 30 decibels. While fenestration for the same group, whose hearing is 50 decibels or worse before operation, offers 10 chances in 100 of the level of 20 decibels or better and 64 in 100 of having a hearing level of 30 decibels or better.

One must conclude from these data that fenestration is the operation of choice for otosclerotic deafness. It is successful in a high percentage of cases and the hearing after one year can be considered permanent. Mobilization has a place in certain instances; the results, however, are inferior to those from fenestration, the closures are greater and the permanency of the result is not known at this time. It is fair to assume that mobilization results will improve as experience is added and as new techniques develop. It is a pity, however, that the experimental changes in technique, I refer to the use of foreign materials (polyethylene and steel struts) in the middle ear, vein graft and pulverization of the footplate, etc., have not been more adequately observed in animals before being used in humans, and one can only hope that no harm is done to those who could be helped with the more certain operation of fenestration.

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LIV

# THE TREATMENT OF MÉNIÈRE'S DISEASE WITH ULTRASONIC WAVES

## FURTHER OBSERVATIONS

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AND

JULES G. WALTNER, M.D.
(by invitation)

NEW YORK, N. Y.

Selective destruction of the organ of equilibrium with preservation of hearing by means of direct application of ultrasonic waves to the exposed bony lateral semicircular canal was first carried out in man by Krejci[6] and then perfected by Arslan.[2-4] The advantages of this method over the other methods of surgical treatment of Ménière's disease are obvious and would make it the treatment of choice in the not inconsiderable number of cases in which medical treatment had been unsuccessful.

In view of the remarkable results reported by Arslan, the apparatus used by him was purchased in Italy.*

The specially constructed sound head (Fig. 1) emits from its tip (active surface 0.2 $cm^2$) a narrow beam of ultrasonic waves with a frequency of 800.000 - 1.000.000 c.p.s. and an intensity of up to 15.0 $w/cm^2$. Lateral transmission of ultrasound is prevented by special shielding and overheating by a cooling system.

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* Available at Apparecchi Scientifici Federici, Via Nirone, Milano, Italy.

In part supported by a grant from the Hayden Fund for the Coakley Memorial Clinic.

From the Department of Otolaryngology, Presbyterian Hospital in the City of New York.

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About one year ago we presented the first and quite encouraging results obtained with this procedure. Similar favorable results were reported by Dubs[5] and by Lumsden.[7] Nineteen additional cases were treated in Presbyterian Hospital until the end of 1958; they are reported in this paper.

The operative routine followed by us is very similar to that described by Arslan. Premedication consists of Seconal® 100 mgm per os, 2 hrs. a.op. and Demerol,® 100 mgm with atropin, 0.3 mgm s.c., 1 hr. a.op.

The operation is carried out under local anesthesia with Xylocaine® 2% with adrenalin 1:100.000. The mastoid is exposed through a retroauricaular incision and entered. Enough cells are removed to get a good exposure of the antrum and of the prominence of the lateral semicircular canal; the incus remains undisturbed.

The tip of the sound head is then applied to the prominence of the lateral semicircular canal. The contact between the two should be as close as possible because interposed air prevents part of the ultrasonic waves from reaching the inner ear. The prominence of the lateral canal is, therefore, under the operating microscope flattened out with a polishing burr. In some cases only the superficial part of the periosteal layer was removed; in others, in order to facilitate the penetration of the ultrasonic waves into the labyrinth, not only the entire periosteal but also the outer part of the enchondral layer was removed until the first signs of a "blue line," indicating the proximity of the canal-lumen, were noticed. However, at present we do not feel that such extensive removal of bone is necessary or desirable as long as a really close contact between the tip of the sound head and the lateral canal is established.

Great care must be taken to apply the ultrasound in such a way that facial nerve and cochlea are not included in the direct path of the beam of ultrasonic waves.

Very careful hemostasis is also essential since even a small amount of blood or other fluid around the tip of the sound head increases the field of irradiation and might endanger the facial nerve or the cochlea.

Nystagmus starts as a rule one to two minutes after onset of the irradiation; if the prominence of the lateral semicircular canal had

Fig. 1.—Soundhead.

been flattened out, the nystagmus is noted earlier, sometimes already after one-half of a minute or even sooner.

The nystagmus must be constantly watched by an assistant, preferably with the help of Frenzel's glasses. At the same time the assistant looks for signs of irritation or paralysis of the facial nerve. If they should appear, the radiation must be stopped immediately.

The initial nystagmus is "irritative" in type, with the quick component directed toward the treated side. It has not been decided yet whether this nystagmus is solely a caloric nystagmus from the heat created by the ultrasound or the result of mechanical vibratory effect of the ultrasound on the sensory neuroepithelium. The average duration of this nystagmus is, according to Arslan, eight to ten minutes. In the majority of our cases, it lasted longer, but this could possibly be due to some technical imperfection of our machine. The homolateral nystagmus is followed by a short period without nystagmus and then frequently by "paralytic" nystagmus directed to the not operated side. This nystagmus is most probably the result of severe

damage to the sensory neuroepithelium by the ultrasonic waves. The irradiation is then continued for another five to ten minutes.

In order to get as complete a destruction as possible of the vestibular end-organs, one should not be content with the disappearance of the "irritative" nystagmus in one particular position of the sound head. The direction of the beam of ultrasonic waves should then be changed towards the vertical canals whereupon one gets again irritative nystagmus which also lasts for five to ten minutes. Then the horizontal and afterwards the vertical canals are radiated a second time to make sure that no more "irritative" nystagmus can be produced in any position of the applicator. If no "paralytic" nystagmus is produced during radiation, it usually appears immediately after termination of the radiation. The average duration of the irradiation in our cases was forty minutes as compared with twenty-five to thirty minutes in Arslan's and Dubs' and thirty minutes in Lumsden's cases.

In one of our patients "paralytic" nystagmus developed immediately after onset of the radiation and persisted in every position of the sound head. The radiation was terminated after thirty-five minutes. Four months later the vestibular responses were absent and the patient was completely free from vertiginous attacks.

In some patients especially those with markedly reduced vestibular responses the usual sequence of nystagmus is often absent; particularly the contralateral, "paralytic" nystagmus may not appear. The radiation is then continued for at least five minutes after disappearance of the homolateral nystagmus. If it does not disappear, the radiation is continued for forty-five to sixty minutes.

The intensity of the radiation depends on the induced nystagmus. If it is marked already with an intensity of 7 - 8 $w/cm^2$, no further increase is necessary. If the nystagmus fails to appear at this intensity, it should be increased to 9 - 10 $w/cm^2$. Higher intensities (up to 15 $w/cm^2$) are rarely necessary and should only be given with great caution.

Since the output of our sound heads is not absolutely constant, we check their function every few minutes by immersing the tip of the applicator into a Petri dish filled with sterile distilled water and watching the ripples produced on the surface of the water by the

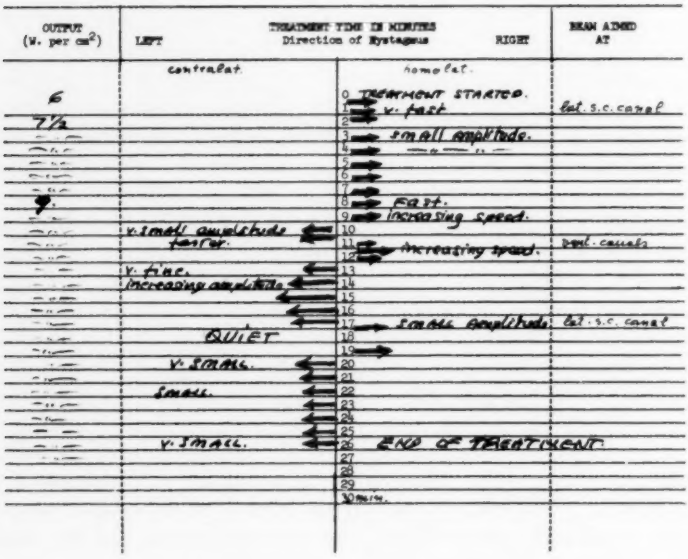


Fig. 2.—Graphic registration of the nystagmus produced by the irradiation.

ultrasound. If they have become weak, the tuning must be adjusted until the ripples again reach maximum intensity. At the termination of the irradiation the wound is closed with clips or sutures.

Epanchin has devised a method of graphic registration of the nystagmus produced by the irradiation which has proven very helpful in reporting and comparing our cases (Fig. 2).

The postoperative course does not show the same marked symptoms as after surgical destruction of the inner ear. There is little or no nausea and vomiting and the nystagmus disappears after twenty-four to forty-eight hours. Some attacks of vertigo may occur during the first postoperative weeks, but they are usually less severe than the preoperative attacks. The unsteadiness after sudden movements of the head disappears completely after three to four months. It

seems that the vestibular end-organs are not always completely and irrevocably destroyed through the radiation even if paralytic nystagmus had been produced. In some of our cases hypoactive responses were still present a few weeks after the operation but were subsequently completely lost after several months. However, in others the vestibular responses were absent for one to two months but returned, although incompletely, after four months.

The only operative complication of consequence, so far reported, is facial paralysis. It was not seen in any of our cases, but in five out of two hundred sixty-five cases by Arslan, in two by Dubs, and in three out of twenty-two operations by Lumsden. The paralysis is usually caused by improper position of the sound head and inclusion of the facial nerve into the field of irradiation or by accumulation of fluid around the tip with subsequent extension of the field of irradiation into the facialis region. In one case of Dubs it was caused by overheating of the tip of the applicator due to a defective cooling mechanism of the sound head. The paralysis eventually cleared up in all the cases but sometimes it took six months before it disappeared completely.

If a facial paralysis should develop in one of our future cases, we would try to shorten the recovery time in the same way as in Bell's palsy with hydrocortisone per os or with intravenous procaine infusions and with anticoagulants.

## REVIEW OF CASES

Altogether twenty-five patients were treated with ultrasound. In twenty-three of them the diagnosis of Ménière's disease was well established. In the remaining two cases the tentative diagnoses were: Hemangioma of the external auditory meatus and middle ear with involvement of the inner ear; old CNS syphilis with syphilitic changes in both inner ears. It might be added that in these two cases the treatment was unsuccessful.

Among the twenty-three patients were seventeen males and six females. In twelve patients the right ear, in nine the left and in two both ears were affected. The ages of the patients varied from 30 to 72 years, the average being 50 years. The average duration of the symptoms before the operation was five years. In one patient the

TABLE I

POSTOPERATIVE VERTIGO, HEARING AND TINNITUS

| | GROUP I. (more than 6 months follow-up) | | GROUP II. (less than 6 months follow-up) | |
|---|---|---|---|---|
| ATTACKS OF VERTIGO | | | | |
| disappeared | 6 | | 5 | |
| markedly improved | 2 | | 5 | |
| recurred | 5 | | | |
| | 13 | | 10 | |
| HEARING | | | | |
| improved | 2 | (7 db, 28 db) | 3 | (10 db, 12 db, 23 db) |
| unchanged | 7 | | 4 | |
| worse | 2 | (14 db, 37 db) | 2 | (8 db, 10 db) |
| lost | 2 | (preop loss 80 db, more than 80 db) | 1 | (preop. loss 50 db) |
| | 13 | | 10 | |
| TINNITUS | | | | |
| disappeared | 1 | | 1 | |
| greatly improved | 4 | | 1 | |
| unchanged | 8 | | 8 | |
| | 13 | | 10 | |

labyrinthine hydrops had developed in an ear which had undergone a radical mastoidectomy twenty-eight years before. In all the cases exhaustive medical treatment had preceded the irradiation with ultrasound.

In order to evaluate the results of the operation properly, the cases were divided into two groups: Group I, comprising thirteen cases, with a follow-up period of six months or more, and Group II, comprising ten cases, with a follow-up period of less than six months.

Table I shows the postoperative results with regard to vertigo, hearing and tinnitus.

Among the thirteen cases of the first group, the attacks of vertigo disappeared completely in six and became so much weaker and modi-

fied in two others that the patients were able to resume their regular work. In the patients with complete cessation of the attacks the vestibular responses were completely absent in four, unreported in one and present in one. Time will only tell if the relief in this case was really permanent. In the cases with modified attacks the responses were markedly hypoactive once and not reported in one instance. In five patients the attacks recurred and persisted several months after the operation.

The cause of the recurrence was in four patients insufficient dosage of the irradiation although in three contralateral nystagmus had been produced for five to fourteen minutes during the radiation. In the fourth patient the homolateral nystagmus had disappeared after irradiation for sixty minutes but no contralateral nystagmus had been produced.

Postoperatively in one of these patients the caloric responses had never completely disappeared; in three they had disappeared temporarily but were again found present, although hypoactive, four months after the irradiation. A second irradiation was given in these four cases after reopening of the mastoid and flattening out of the prominence of the lateral semicircular canal. In all of them, followed up so far for about three to four months, the attacks of vertigo have completely disappeared.

In the fifth case the vestibular responses had remained completely absent five months after the irradiation, at the time when the attacks of vertigo recurred. Since this patient had a bilateral endolymphatic hydrops and since the hearing in the other, not operated, ear started showing fluctuations, it is assumed that the attacks were caused by the not operated ear and irradiation of this labyrinth is now considered. Such a procedure is, according to Arslan, only very seldom necessary, but was successfully carried out by him after an interval of six months in three of his two hundred sixty-five patients.

In the second group the attacks of vertigo have disappeared completely in five and greatly improved in five patients. The vestibular responses were rechecked in three of the cases with complete disappearance of vertigo. They were absent in two and hypoactive

in one. In two of the improved patients the vestibular responses were absent, in two they were hypoactive and in one unreported.

The hearing improved in the first group in two, remained unchanged in seven, got worse in two and was completely lost in two cases. One of them had a preoperative hearing loss of 80 db for 500 and 1000 dv and no hearing for 2000 dv. One month later the hearing decreased by 10 db for 500 and 1000 dv and two months later the hearing was completely and permanently lost for all frequencies. The second case is one of the four which received a second irradiation with ultrasonic waves. This patient, a man of 72 years, had been suffering from bilateral labyrinthine hydrops for many years and had a hearing loss averaging 70 db on the right and 80 db on the left ear. After the first radiation the hearing had remained unchanged but the vestibular responses had never completely disappeared. Since the attacks of vertigo started to recur eight months postoperatively, a second radiation was performed thirteen months after the first one. Three months later, there was no recurrence of the vertiginous attacks and the vestibular responses were completely absent in the operated ear but the small amount of residual hearing had also gone.

Among the three other cases, the hearing improved by 7 and 8 db after the second radiation in two and remained unchanged in one.

In the second group the hearing so far has improved in three, remained unchanged in four, gotten worse in two patients and completely lost in one. This patient, a man of 63 years, had been suffering from a left-sided labyrinthine hydrops for about twenty years. His preoperative hearing loss for the frequencies 250-4000 dv averaged 50 db. Preceding the irradiation the prominence of the lateral semicircular canal had been flattened out somewhat more than usually until the "blue line" had become clearly visible. The radiation was carried out with an intensity of 7 to 9 $w/cm^2$ for 48 minutes. At first homolateral nystagmus appeared lasting for 35 minutes and was followed by contralateral nystagmus. Four months later the dizzy spells had become much less frequent and very much milder. The tinnitus remained unchanged. The vestibular responses were absent and the hearing completely lost.

The tinnitus disappeared in the first group completely only once together with a very great improvement of the vertigo. It became

TABLE II

RELATIONSHIP BETWEEN POSTOPERATIVE VERTIGO AND HEARING

| | VERTIGO | | HEARING | | | |
|---|---|---|---|---|---|---|
| | | | better | unchanged | worse | lost |
| GROUP I | absent | 6 | 2 | 4 | – | – |
| | improved | 2 | – | 1 | – | 1 |
| | recurred | 5 | – | 1 | 4 | – |
| | | 13 | | | | |
| GROUP II | absent | 5 | 1 | 2 | 2 | – |
| | improved | 5 | 2 | 2 | – | 1 |
| | | 10 | | | | |

considerably weaker and at times hardly noticeable four times together with complete disappearance of the vertigo; in eight patients the tinnitus remained unchanged. Only in two of them did the vertigo completely disappear; in one it improved considerably, and in another case the vertiginous attacks recurred due to active changes in the other labyrinth. In the remaining four cases, a second radiation became necessary because of recurrent attacks of vertigo and the tinnitus afterwards improved considerably in one of them.

In the second group, the tinnitus disappeared in one case together with the vertigo; it greatly improved in one, again with disappearance of the vertigo, and remained unchanged in eight cases. In four of the latter, there has been so far no recurrence of the vertiginous attacks; in four they became much less intense and frequent.

A comparison of the hearing in successfully and in unsuccessfully irradiated cases shows the following (Table II):

In the six cases of the first group with disappearance of the attacks, the hearing was better in two and unchanged in four patients. In two patients with marked improvement of the attacks the hearing was unchanged once and completely lost once. In the first patients with recurrence of the attacks the hearing was worse in four cases and unchanged in one.

In the second group the hearing in the five cases with disappearance of the vertigo was improved once, unchanged twice and worse twice. In the five patients with marked amelioration of the attacks the hearing was improved twice and unchanged twice and completely lost once.

## COMMENT

The discussion of the results is confined to the cases of the first group with a follow-up period of six months or more because we feel that a shorter follow-up period does not permit completely valid conclusions. The results with regard to the cure of the vertigo (eliminated in six and greatly ameliorated in two out of a total of thirteen patients) do not seem very impressive at first sight. However, one must realize that the cause of failure was insufficient dosage in four and pathology in the other labyrinth in one patient. These cases might still become successful after additional irradiation of the originally treated or irradiation of the other labyrinth. As a matter of fact, all four irradiated patients are free from vertiginous attacks for three to four months after the second irradiation.

Application of an insufficient amount of ultrasound seems the almost exclusive cause of failure not only in our own but also in Dubs' and Lumsden's cases.

It is quite possible that with increased experience under-treatment will become less frequent and that then the percentage of our successful cases will eventually approach the 95% reported by Arslan.

With regard to the effect of the radiation on the hearing we still think that neither the improvement nor the deterioration observed in some of the cases exceeds the fluctuations frequently noted in cochlear hydrops. A similar opinion was lately expressed by Lumsden.

The complete loss of hearing which gradually developed in two patients with a severe preoperative hearing loss (80 db or more) could be explained by the assumption that already severely damaged cochlear end-organs are less resistant to the action of the ultrasound than normal end-organs. The complete loss in one of the patients of the second group who had fairly good preoperative hearing (average loss 50 db) might be due to the fact that the bony wall of the lateral

canal had been taken down a little bit more than in the other cases. A larger amount of ultrasound might have penetrated into the labyrinthine cavities. It is, therefore, suggested that not more bone should be taken off from the prominence of the lateral semicircular canal than necessary to establish close contact between the tip of the applicator and the canal. At any rate, the fact that a complete loss occurred three times for one reason or another makes irradiation of the ear with the better hearing in patients with a severe bilateral hearing loss less advisable.

The fact that the hearing in the six cases with complete cessation of the vertiginous attacks was better in two and unchanged in four cases, but in the five cases with recurrence of the attacks, worse four times and unchanged once deserves closer attention. It is according to Arslan conceivable that the effect of the ultra sound is not solely due to destruction of the neurosensorial elements in the cristae and maculae but also to an improvement of the endolymphatic circulation with subsequent diminution or even complete cessation of the fluctuations of the endolymphatic pressure which account for the deterioration of hearing during and shortly after the vertiginous attacks. However, in some cases the pressure fluctuations seem to continue. One of Dubs' patients in whom the vertigo had been completely eliminated still continued having attacks of pressure in the head, tinnitus and decreased hearing in the irradiated ear.

Complete or almost complete relief from tinnitus was achieved in accordance with the results of Lumsden in more than one-third of the patients whereas Arslan reports considerable improvement in two-thirds of his cases. Although this figure is not too impressive, it is better than that obtained with medical treatment and not worse than the results from destructive methods of surgical treatment.

## SUMMARY AND CONCLUSIONS

The technique of the radiation of the labyrinth with ultrasonic waves is described and the results in twenty-three patients with endolymphatic hydrops analyzed.

In six out of thirteen patients followed for more than six months the vertiginous attacks were completely eliminated and in two greatly improved. Failure of the treatment in four cases was due to insuf-

ficient dosage, but all these patients are now, three to four months after a second radiation, free from attacks. In another case the recurrence of the attacks was caused by the not radiated labyrinth.

No definite influence of the radiation was noted upon the hearing, except in two patients with a very marked and in one with a less severe preoperative hearing loss. In all of them the hearing was completely lost in the first months after radiation or re-radiation. Ultrasonic treatment of the better hearing ear seems, therefore, inadvisable in patients with a severe bilateral neurosensory hearing loss.

Complete or almost complete relief from tinnitus was achieved in more than one-third of the patients, a figure which is better than that obtained with medical treatment and not worse than the results with destructive methods of surgical treatment.

Facial paralysis, the only complication of consequence of this treatment, was not observed in our series of cases.

Experience with many more cases and over a much longer period of time will be necessary for a final evaluation of the treatment of endolymphatic hydrops with ultrasonic waves. The additional experience gained during the last year tends to confirm the opinion expressed in a preliminary report and shared by Dubs and by Lumsden, that the results are so encouraging that this method will probably not only replace the present destructive surgical methods but will also be used in many cases in which at present medical treatment seems the only possibility. In full agreement with the two authors it is felt that with increased experience the percentage of primary successes will become higher and will eventually approach the excellent results reported by Arslan.

10 East 85th St.

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The authors are greatly indebted to Prof. Dr. M. Arslan, Padova, Italy, for his continued interest in their work and his freely given and invaluable advice.

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LV

# PRESBYACUSIS

## THE AGING EAR

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NEW YORK

Saints or sinners, mice or men, all animals who possess hearing will, if they live long enough, suffer from what we call presbyacusis. This statement is a broad generalization but Hallowell Davis thinks it is good although only in man, cat, dog and guinea pig has it been experimentally proven. I refer to the work of Guild et al,[1] Schuknecht;[2] Pestalozza, Davis, Eldredge and Covell and Rogers.[3,4]

We are approaching the time when half of us will have presbyacusis because nearly half of our population will be over 50 years of age. It is important, particularly for the otologist, to understand the effect of these facts upon his patients and for that matter upon himself.

In this brief discussion I shall present a few facts and a few ideas, being fully cognizant that an idea is not an hypothesis, a concept is not a theory, and that coincidence and incidence or association do not necessarily mean causation. However, without ideas there is no hypothesis, no concept and no progress.

### DEFINITION

Presbyacusis, or presbycusis, also presbykousis, is a diminishing hearing acuity incident to advancing years due to a progressing loss of function, mainly in the neural apparatus of hearing (peripheral, central or cortical, singly or combined, continuing or intermittent).

This definition suggests that the hearing loss corresponds to the number of years lived. It is somewhat misleading as I shall explain.

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Read at the Ninety-second Annual Meeting of the American Otological Society, Hot Springs, Va., March 1959.

A synonym for presbyacusis is "old age deafness."

In order to lessen the opprobrium of either of these terms the term "normal aging" has been proposed to contrast it to the pathologic groups in which arteriosclerosis of the cerebral vessels, brain softening or arteriosclerotic psychoses or dementias are prominent entities, to name a few. But it is rare indeed for old people not to have arteriosclerosis and other vascular disorders. Even minor vascular episodes, even microscopic lesions in the cortex, affect function. Why such lesions do not sooner reveal their presence is a mystery.

## ETIOLOGY AND PATHOLOGY

The aging process is so little understood that it is a weak hook upon which to hang the etiology of disorders or diseases occurring in older people. What is old age? Is it simply any age over 40 or 50, 60, 70 or 80? Or is it some somatopsychic change affecting the body in whole or mainly in certain parts? The tissues of the body show aging changes at different times and with differing speeds and degrees. Biologically our aging is spotty. Although it may be said that slow loss of function in any important organ is always associated with metabolic deficiencies such a loss is not necessarily due to biological or chronological aging, per se.

Some parts of the body are adult in size and may be said to be old even before we are born. The otic capsule is one such part. Its growth is more maturing than aging. The otic capsule at birth, or soon thereafter, is the most mature in size and function, and the most permanent in stability of appearance, of any structure of the body, but like all structures it inevitably undergoes slow changes with time. The most notable change in old age is osteoporosis. The other bones, and incidentally the teeth which at first thought appear remarkably stable, eventually suffer marked changes being commonly subjected to more trauma, infection and neurovascular vicissitudes than the petrous bone and therefore they may be said to reveal more recognizable so-called changes incident to aging, i.e., more "presbyosia" and "presbydontia" respectively, than the ear bones. The nerves, the ganglia, and the neural end organs age after attaining their maximum development, probably before 21 years of age, and the brain cortex may be a few years later.

Heredity sets the pattern and influences the incidence and degrees of health and disease throughout life but it is not strictly a cause, and its influence may be strengthened or weakened. However, we know that in many families through several generations, and even at approximately the same ages, similar disorders of function occur, one of which is presbyacusis. However, occasionally even in identical twins, and in the right and left ears of a person the year of onset of presbyacusis and the rate of loss of hearing may differ widely.

Severe strains, especially recurrent and continuing strains from emotional episodes, such as fright, grief and frustration, poisonous drugs such as quinine and the salicylates, some alkaloids, antibiotics (dihydro-streptomycin), over-exertions, bacterial and virus infections, acoustic, psychic and other traumas, electric shock, endocrine and metabolic disorders (hypothyroidism or hypometabolism) pregnancy, vitamin deficiencies, hyperoxia, hypoxia, exposure to cold, allergies, thromboses and vaso-spasms and many other disorders, have been observed to precede the onset of presbyacusis and for that matter other types of neural deafness, even total deafness. With few exceptions my presbyacusis patients give a history of somatopsychic strains correlated with the subsequent onset of their presbyacusis.

I have noticed that if both parents suffer from an early presbyacusis their offspring appear to inherit a similar deafness both in degree and in timing more often than if only one parent was so affected. Dolowitz has shown this nicely. During the passage of years, irrespective of heredity, many people suffer from various types of neural or impedance lesions of the ear which of course are then superimposed upon and increase the hearing losses incident to aging. Such lesions diminish resistance to subsequent insults from any cause.

How are we to differentiate the different types? It would seem that at least we can exclude presbyacusis unless the hearing loss is progressive.

Although presbyacusis is roughly correlated to age and the general medical and otological history I have many patients in their late 70's and some in their 80's who reveal no more than a 10 db loss at any of the frequencies up to and including 8000. Incidentally these patients are remarkably free from tinnitus and are well adjusted, emotionally stable people. Vertigo in this group is conspicuous by its

TABLE I

***Incidence in Siblings.*** **A special position in the family, and sex, appear to be factors in the timing and severity of several types of neural deafness including presbyacusis. Looking over the histories of 666 consecutively examined patients with neural deafness (each having one or more siblings), I find that 80 per cent were over 30 years of age at the date of my first examination, and that 70 per cent gave a history of deafness beginning after they were 30 years of age.**

| | WERE THE ELDEST | RATIO | WERE THE | RATIO | WERE THE | RATIO | WERE THE |
|---|---|---|---|---|---|---|---|
| In 82 females with 1 sib. | 55 | 2:1 | 27 younger | | | | |
| In 89 males with 1 sib. | 64 | 2.6:1 | 25 younger | | | | |
| In 62 females with 2 sibs. | 33 | 2:1 | 17 second eldest | 1.5:1 | 12 youngest | | |
| In 70 males with 2 sibs. | 38 | 2.3:1 | 16 second eldest | 1:1 | 16 youngest | | |
| In 52 females with 3 sibs. | 24 | 3:1 | 8 second eldest | 1:1 | 7 third eldest | 1:2 | 13 youngest |
| In 79 males with 3 sibs. | 35 | 1.7:1 | 21 second eldest | 2:1 | 13 third eldest | 1.3:1 | 10 youngest |
| In 120 females with 4 or more sibs. | 59 | 4.2:1 | 14 second eldest | 1:1 | 14 third eldest | 2:1 | 6 fourth eldest |
| | | | | | | | 9 fifth eldest |
| | | | | | | to | 7 sixth eldest |
| | | | | | | | 4 seventh eldest |
| | | | | | | 14:1 | 4 eighth eldest |
| | | | | | | | 1 ninth eldest |
| | | | | | | | 2 tenth (the youngest) |
| In 112 males with 4 or more sibs. | 57 | 4:1 | 14 second eldest | 1:1 | 12 third eldest | 1.5:1 | 8 fourth eldest |
| | | | | | | | 7 fifth eldest |
| | | | | | | to | 5 sixth eldest |
| | | | | | | | 4 seventh eldest |
| | | | | | | 12:1 | 3 eighth eldest |
| | | | | | | | 1 ninth eldest |
| | | | | | | | 1 thirteenth (the youngest) |

666 total number of patients

absence although some do mention occasional unsteadiness or dizziness. But in spite of excellent hearing for pure tones they usually suspect that they do not hear as well as formerly, particularly foreign accents, when in noisy environments, and when not listening. However you are often surprised how well "Grandma can hear when she wants to hear." I will discuss this anon. The lack of discrimination so often present in old people Carhart calls "phonemic regression."

Notice that there are many more patients in the groups of eldest siblings, a lesser percentage in the groups of the second eldest siblings, and with one exception a lesser percentage in the groups of third eldest siblings. Notice that with an exception in one female group the numbers in each group diminished with age. Notice that in families with five or more siblings the number of patients in the oldest female and male sibling groups was over four times that in the next in age sibling groups, and the ratio between each older and next older group diminished with the age of the siblings. In other words, there was not only a definite relationship to chronological age but the ratios of the elder of any two siblings to the next of age followed closely this pattern of decline even in families with as many as thirteen siblings. This was to be expected. It was due in large part to lesions which we associate with presbyacusis. The great majority of these patients did have presbyacusis.

The tabulations contain other interesting data but a larger sample should be obtained before discussing them.

The histopathology of marked presbyacusis may show degenerations in the spiral ganglion and in Corti's organ similar to those frequently found in young people with similar patterns of neural deafness. The audiograms may have been identical. Does this mean that the deafness is of similar origin in spite of differences in chronological age, and in spite of the fact that the deafness in the young has usually not been progressive? Although lesions may appear similar their etiology may be different, and vice versa, but I believe in this case the basic causes in both the young and the aging are similar insofar as they are dependent upon a disordered metabolism, particularly a disordered oxygen supply.

Anoxia is caused by any interference with the supply of oxygen from the blood, such as occurs with spasm or narrowing of the arteri-

oles or arteriolar capillary sphincters, an insufficient rate of flow, pressure, intravascular impedance lesions, or other similar factors. An important reason for the spottiness of lesions is that every major artery system in the body contains its own neurovascular response mechanism, and may react differently even to similar stimuli and in differing degrees.

The arteries are muscular tubes, they are not inert channels, they normally maintain a tone and vary their lumens by muscular contractions and relaxations as well as by adjusting to the changing pulsing pressure of the blood stream. The smaller arterioles are so small that there is hardly room for a single red blood cell to pass. If two red blood cells are stuck together face to face, 50 per cent of their outer surfaces is smothered. If ten cells are stuck together, 90 per cent of their outer surfaces is smothered. Clumping of blood cells must cause a local anoxia whether or not there is some relief from nearby anastomosing vessels because the blood from the anastomosing vessels also is clumped. Also remember that in Corti's organ the arteries are terminal.

No one knows just why the blood cells do not always stick together. They are protein bodies and protein is sticky. The blood contains lipoids and all fatty substances are sticky. It may be that when the rate of blood flow is sufficiently rapid the cells tumble along and do not tarry long enough to get stuck together. In deep sleep and in hibernation I suspect that the blood cells do tend to stick together, but in these states the oxygen supply-demand ratio is low and no harm results unless there is some pathology. Maybe electrical potentials or enzymotic factors keep them apart. The constant rhythmic or intermittent contractions and relaxations of the blood vessels and Brownian agitation play a part, the latter varying with the amplitude of movement, and the viscosity of the plasma. Severe or prolonged spasms would have an opposite effect; they definitely are a cause of intravascular agglutinations in the blood. Probably all of these factors and more play a part.

One factor that stands out in presbyacusis is that in no instance, even in healthful adults, have I failed to detect a considerable degree of intravascular agglutination of the blood cells. The same holds for young people with progressive neural deafness. This by no means implies that sludging is the only etiological factor, or that sludge can

not exist for a while without presbyacusis. It does to my mind imply that it is an important factor. It is the only in vivo sign that is always present, the only patho-physiology which makes much sense as a basic etiological factor and it ties in with emotional strains and hyper-epinephrin reactions. Incidentally sludging often changes from day to day and even from hour to hour. So does the acuity of hearing.

Many investigators have shown that cochlear microphonics, action potentials and D.C. resting potentials, are dependent upon oxygen supply.

When oxygen lack occurs other metabolites also are affected. Moreover the mechanisms for getting rid of the wastes are faulty.

Ten years ago Wever et al[5] experimentally measured the loss of the cochlear potentials in animals with varying degrees of oxygen lack. Only severe anoxia caused the losses and all frequencies were affected alike. Wever also showed that the lowered responses did not progress regularly but stabilized at plateaus of loss, diminishing further only after prolonged periods or more severe exposure to the anoxia. The oxygen supply-demand ratio evidently varied at different levels of functioning. The loss in response was reversible if the anoxia was not too long endured, or too severe.

Paradoxically Fernandez and Alzate[6] found that microscopically there appeared to be no evidence of degeneration in Corti's organ in the animals they examined after asphyxia was repeated at one hour intervals, each bout lasting at least three minutes, although there was an apparent permanent depression of both cochlea microphonics and neural components. Even greater exposures showed no evidence histologically. This does not mean that none occurred. It means that the methods employed were not capable of detecting the changes.

Instead of showing you the average losses by decades in air and bone conduction in the population at large I will show you the changes which occurred in the hearing of a man who has been tested audiometrically over a greater period of time than anyone else in the world. This person was tested many times a year but I omit many tests because they take up too much space and do not reveal much of importance (Table II).

TABLE II

AUDIOGRAMS FROM 1921 TO 1959

| | 125 | 250 | 500 | 1000 | 2000 | 4000 | 8000 | 9000 | 16000 | 125 | 250 | 500 | 1000 | 2000 | 4000 | 8000 | 9000 | 16000 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1-A | | | | | | | | | | | | | | | | | | | |
| 1921 | 5 | 0 | 0 | 0 | 5 | 10 | 10 | | 10 | −10 | −10 | −10 | −10 | 10 | 5 | 25 | | 20 | 48 yrs. old |
| 1924 | 0 | 5 | 5 | 0 | 5 | 5 | 15 | | 15 | 0 | −5 | −5 | −10 | 10 | 5 | 30 | | 25 | |
| 1927 | 5 | 5 | 0 | −5 | −5 | 0 | 5 | 30 | | 0 | −5 | −5 | −5 | 15 | 10 | 5 | 35 | | |
| 1930 | 5 | 0 | 0 | −5 | 5 | 5 | 10 | 30 | 20 | 0 | 0 | 0 | −5 | 15 | 15 | 10 | 35 | 30 | ) Emotional |
| 1932 | 5 | 5 | 0 | 0 | 5 | 10 | 10 | 30 | 20 | 0 | 0 | 0 | 0 | 15 | 20 | 15 | 35 | | ) strains |
| 1934 | 0 | 5 | −5 | 0 | 10 | 5 | 5 | | 20 | 0 | −5 | −5 | −10 | 20 | 25 | 15 | | 40 | Less strain |
| 1936 | 0 | 0 | 10 | 5 | 15 | 15 | 20 | 30 | nil | 0 | −5 | 0 | −5 | 20 | 25 | 30 | 40 | nil | |
| | 0 | 0 | −5 | −5 | 0 | 5 | 5 | | | 0 | 0 | −5 | −5 | 20 | 25 | 15 | | | |
| 1937 | 5 | 10 | 5 | 5 | 15 | 20 | 30 | 20 | | 0 | 5 | 15 | 15 | 15 | 20 | 30 | | | 64 yrs. old |
| 1938 | 0 | 5 | 5 | 15 | 10 | 35 | 35 | | | 5 | 0 | 0 | −5 | 0 | 35 | 10 | | | |
| 1939 | −10 | 0 | −5 | −5 | −5 | 0 | 20 | | | −5 | −5 | −5 | 0 | 0 | 5 | 30 | | | I.C. removed |
| 1940 | 10 | 15 | 15 | 15 | 20 | 50 | Masking experiments | | | | | | | | | | | | |
| | 0 | 0 | 0 | 5 | 5 | 10 | 35 | 30 | | 0 | 5 | −5 | −15 | 0 | 10 | 30 | 25 | | |
| 1941 | −5 | 0 | 0 | 0 | −10 | 0 | 20 | | | 0 | 0 | 0 | 0 | 0 | 0 | 35 | | | |
| 1944 | 5 | 5 | 5 | 0 | 5 | 15 | 25 | 30 | | 10 | 10 | 5 | 0 | 5 | 30 | 35 | 45 | | ) 71 yrs. old |
| B.C. | | 0 | −10 | −10 | 0 | 15 | 15 | 30 | | | 0 | −5 | 10 | 10 | 30 | 30 | 35 | | ) B.M.R. −8 to −16 |
| WE 6-A | | | | | | | | | | | | | | | | | | | |
| 1948 | 0 | 0 | 5 | 0 | 5 | 30 | 35 | | | 10 | 15 | 0 | −5 | 15 | 50 | 55 | | | |
| 1951 | 0 | 5 | 5 | −10 | 15 | 35 | 60 | | | 10 | 10 | 5 | −5 | 15 | 55 | 55 | | | |
| 1953 | 10 | 15 | 10 | −5 | 20 | 50 | nil | | | 20 | 20 | 10 | 0 | 25 | 55 | 70 | | | 80 yrs. old |
| 1954 | 15 | 15 | 10 | 0 | 20 | 50 | 55 | | | 20 | 20 | 10 | −5 | 20 | 60 | 55 | | | |
| 1955 | 20 | 20 | 15 | 0 | 20 | 55 | nil | | | 25 | 30 | 15 | 0 | 20 | 55 | 65 | | | Nasopharyngitis |
| WE 6-PB | | | | | | | | | | | | | | | | | | | |
| 1956 | 15 | 20 | 15 | 0 | 30 | 55 | nil | | | 20 | 30 | 10 | 0 | 30 | 55 | nil | | | |
| 1958 | 35 | 40 | 40 | 25 | 50 | 75 | nil | | | 20 | 15 | 10 | 15 | 30 | 60 | 70 | | | I.C. right |
| | 15 | 15 | 15 | 0 | 25 | 70 | 70 | | | 15 | 15 | 10 | 15 | 30 | 60 | 70 | | | |
| 1959 | 20 | 25 | 15 | 0 | 25 | 65 | 70 | | | 30 | 30 | 15 | 10 | 25 | 70 | nil | | | Stuffy. 86 yrs. old |
| B.C. | 5 | 0 | 5 | 10 | 5 | nil | | | | 5 | 5 | 10 | 10 | 5 | nil | | | | |

Fifteen or twenty years before the advent of the audiometer several severe acoustic traumas were endured, one of which caused total deafness for several minutes. The right ear recovered first and the left, the more exposed ear, a few seconds later. The patient is right handed and was shooting a high powered rifle when a gun was exploded, its muzzle being close behind and on the left side of the patient. You will notice that no immediate marked permanent loss of hearing resulted, and that there was no "dip" at or near 4000 cycles. However, you will also notice that there was considerable loss at 9000 and 16,000 at the time of the first audiometric testing and that these losses persisted and later were increased. These losses probably set the stage for the subsequent presbyacusis losses and rendered the ears earlier susceptible to such.

You will notice that following emotional strains, around 1930, the hearing diminished considerably for the high tones in both ears but that the low tones were hardly, if any, affected. Was this the beginning of presbyacusis? The patient was 57 years of age in 1930 and this is a late date for presbyacusis to begin. However, in 1921, when the patient was 48 years of age, there was a loss in the right ear of 10 db at all of the higher frequencies, and a loss in the left ear of 10 to 25 db. Incidentally at that age the left ear had better hearing for the low tones than did the right ear. Did this patient have presbyacusis at this early date? I would be inclined to suspect so, even though there was considerable improvement after 1932, and that the hearing did not progressively deteriorate further until 1937. Even after 1937, when the patient was 64 years old, there was no progression in the deafness for several years although the 16,000 frequency could not be heard after 62 years of age.

It will be noted that in 1948, when the patient was 75 years of age, there was a further loss in the high tones in both ears and that the low tones also were no longer above the zero line, except at 1000 cycles in the left ear.

The bone conduction is only given for 1944 when it coincided pretty closely with the air conduction losses, and in 1959 when in spite of the considerable losses by air conduction it was near normal up to and including 2000. Recruitment was not detected in these middle and low frequencies but was present in the frequencies above 2000. This indicates that the lower frequency losses were not neural

and maybe therefore not a part of the presbyacusis. But there is no good reason why the losses in presbyacusis have to be wholly neural.

I will not discuss the average threshold audiogram curves of people in varying decades of life. They include many people with various impedance and neural lesions present long before they were tested. They do not furnish us with sufficient information as to the etiology of what we call "presbyacusis." As I showed, 26 years ago, in a paper on "The Effect of Severe Illness Upon the Hearing,"[7] there are aging people in their 60's, 70's, 80's and even above who in spite of their old age and arteriosclerosis, possess excellent hearing (some perfect hearing) for all the clinical audiometer frequencies, sometimes for those above 4000 (even 8000).

## DIAGNOSIS

It is difficult to determine the exact date when presbyacusis begins but when well established it is easy to diagnose it. The patient usually does this himself. An important method of detection is to think about it, to keep it in mind.

It is difficult to diagnose monaural presbyacusis but proper audiometric testing at intervals will aid in diagnosis unless there are other disorders of the hearing mechanism which are blamed for the progressing deafness.

There is a notion that recruitment is not present in presbyacusis but with few exceptions I have found it present. In instances where patients complain about the annoyance of loud environmental sounds, this is one sign of recruitment. When there is a neural hearing loss but no sensed recruitment of loudness I explain it by lesions central to Corti's organ, some neural impedance in the pathways in the brain stem, a feed back, or some deficiency in the receptor mechanisms in the cortex. Any of these might prevent a patient from sensing a recruitment of loudness, even though there was a recruitment of potentials in Corti's organ.

An elevation in the pitch of a tone as it is increased in loudness is an indication of recruitment and in such instances the minimum detectable increment of pitch is diminished. This may be called a

"recruitment of tone." I believe it occurs in neural deafness whether or not there is a recruitment in loudness so long as there is a recruitment of potentials in the end organ.

## MANAGEMENT

Little or nothing has heretofore been accomplished in prevention, or cure of presbyacusis, but a start has been made in management.

Properly obtained threshold audiograms and above threshold responses enable us to better determine when a hearing aid is indicated than in the past. But in spite of the logic of our choice the presbyasusis patient may not accept the aid. His preferences but not his prejudices or whims should be followed. Usually a flat response appears more natural and therefore more acceptable than any fancy so-called elevating the high tones which actually only depresses the lower tones and necessitates an excess of amplification and consequently more distortion.

Severe presbyacusis is frequently difficult to help satisfactorily with a monaural aid. Binaural hearing aids are preferable and satisfy many people who will not tolerate monaural aids. A word of caution, train your patient to use the aids properly, to turn the loudness up and down automatically. Too much intensity can cause fatigues and further neural degeneration in Corti's organ.

To avoid over-resentment and emotional repercussions, patients should be conditioned to accept hearing aids before the time arrives when they should be used. If they do not adjust to the use of aids they are going to lessen their happiness in living and be a greater nuisance to themselves and to their families and friends than is necessary. This is really preventive "auditory training" or more accurately "training in listening." Carhart has measured how much the intelligibility score may be improved by proper training.

## TREATMENT

The chief roadblocks to successful treatment are failure to make an early diagnosis, and failure to realize that we often can be of assistance in several ways.

We possess means by which the intravascular agglutinations of the blood can be diminished but none have had a permanent effect. The more powerful drugs cannot be used indefinitely; many are dangerous. We must remember that intravascular agglutinates are not the same as clotting of the blood, but that the masses although they contain no fibrin do clog the vascular tubing for longer or shorter periods and cause anoxia.

We have been experimenting with several of the safer medications which appear to have an anti-agglutination effect but have not accumulated sufficient material to warrant a definite stand as to their efficacy. I will say that in no instance have they caused any side effects or any damage.

When in addition we have lessened the emotional factor in these cases and the tinnitus has stopped or diminished, the hearing has often improved to some extent and stabilized for long periods of time.

Hypothyroidism occurs more frequently in women than in men. It reduces the oxidating rate; it diminishes the supply-demand ratio, and may cause extracellular edema and accumulations of serum in serous sacs. Edema may cause deafness, tinnitus and dizziness and an increase of cholesterol in the blood stream.

Even when there appears to be no general hypothyroidism or hypometabolism there may be local hypometabolism and inevitably when there is an anoxia, which may account for the fact that small doses of thyroid frequently help and sometimes dramatically. Antiepinephrin medication, nicotinic acid, nitroglycerine, the iodides and many other drugs seem indicated in some instances, but I will not at this time discuss treatment further.

It is important not to be dogmatic in these matters, to say it can't be done. Keep trying with ever newer and newer ideas. Bear in mind that old ideas, old definitions and old concepts are not enough.

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LVI

# NIHIL SUB SOLE NOVUM

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Because of its bone-locked location within the petrosa and because of its minute and intricate structure, the internal as well as the middle ear remained as terrae incognitae for many years. The internal ear's dual physiological functions apparently remained unguessed for almost another three centuries.

The history of the middle and internal ears presents the fascinating story of a long voyage of discovery that has not reached its conclusion. At least three episodes in this odyssey have evoked my curiosity and my interest. One of them indicates a medical hoax; two of them are far from hoaxes and are similar enough to point a very powerful object lesson to modern day physicians. All of them seem to have been little noticed or totally unnoticed through the years although they call to me in unmistakable terms. Developing and in some measure clarifying these episodes has been an interesting and fascinating period of enjoyment to me. May I share this interest and fascination with you?

Vesalius' knowledge of the middle and internal ears was practically nil. Here (Fig. 1) is his illustration of a section of the temporal bone from his De humani fabrica (2nd edition [1555], p. 43). Any evidence of the cochlea or semicircular canals, if present, is confused with the mastoid cells. The VII and VIII cranial nerves, then known collectively as the fifth pair, are shown as expanding aimlessly through these cells to enwrap the tympanic cavity. Only the malleus and incus are shown and they are articulated incorrectly. Since this is the second and corrected edition of the Fabrica it must state definitely the extent of his knowledge at the time. In a cordial letter written to Fallopius, his successor to the chair of anatomy at Padua, on the publication of Fallopius' Observationes Anatomicae in 1561

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he told of having recognized the stapes only after its existence had been noted by Ingrassia (vide infra). But no mention is made in this letter of any knowledge of any other portion of the middle or internal ear.[1]

At the moment we must recall that Vesalius, by his dissections and his fierce espousal of the discoveries made possible by them, is remembered for having broken the chains of the *false* teachings of Galenism which had bound and hampered medical progress for thirteen centuries. But he is quite as strong in his espousal of the many *facts* discovered by Galen. These facts are legion, and being facts they are accepted to this day. Galen when measured against the background of his time stands as the greatest physician of all time. This Visalius recognized.

Fallopius in his Observationes[2] gives a fairly accurate description of the osseus structures of the internal ear. He names the labyrinth, describes the cochlea as of three turns and he specifically mentions and describes the vestibule and the semicircular canals. He is accorded priority in the discovery of the canals. The first accurate pictorial presentation of the internal ear is to be found in Casserius' Organus Auditus.[3]

We come now to a third pioneer in anatomy. His name is used more frequently than any other by otologists because of its connection with the structure which he described accurately for the first time although it had been recognized centuries earlier—Bartolomeus Eustachius. It is about him that the first two episodes revolve.

Eustachius was professor of anatomy at Rome. As such he became personal physician to Pope Sixtus IV. Since Galenism was accepted as the correct system of medical thought by the Church, Eustachius bowed to clerical authority and failed woefully to evince the bold striving for freedom of thought shown by both Vesalius and Fallopius at Padua. The proximity of Eustachius to the center of religious authority, with personal appointments and emoluments at stake, and the distance of Padua which in those times was considerable may well account for this difference. If so, Eustachus has paid severely for obsequiousness.

In 1552 the engraving of 39 copper plates by Giulio de Musi made from dissections by Eustachius for a contemplated work on anatomy was completed. For these plates Eustachius left no line of description

Figure 1

Figure 2

Figure 3

or commentary with the exception of the first eight additional plates to be mentioned immediately. These 47 plates collectively are known to us today only as the Tabulae Anatomicae—the Anatomical Plates.

All of the plates of the Tabulae Anatomicae probably were suppressed and segregated in the Vatican Library by Pope Sixtus IV, although they may have been withheld voluntarily by Eustachius in deference to theological views concerning contradictions of Galenism. At any rate they disappeared and remained unknown until just before 1714 when they came to light again during the Papacy of Clement XI and were presented by him to his personal physician, Giovanni Maria Lancisi. Lancisi published them in 1714 with his own notes and commentaries at Rome.[4] Had they been published when they were engraved they would have taken precedence over those of Vesalius for "they are more accurate than those of Vesalius."[5] This was indeed a price to pay!*

* Mention had been made repeatedly in the literature of the dry, stiff, manikin-like appearance of the Eustachian plates as compared to those of Vesalius even though they are the more accurate. Responsibility for this has been placed upon de Musi because prior to these plates he had worked only with architectural plates.[6] But there exists another and perhaps more reasonable explanation. In October, 1958, in discussing this paper with Dr. Ralph Major, Professor Emeritus, and Dr. L. R. C. Agnew, Professor and Chairman of the Department of Medical History at the University of Kansas Medical Center at Kansas City, they showed me a manuscript in the History of Medicine Collection, Clendenning Medical Library. This manuscript is undated and unsigned but it consists of the notes taken by an unknown medical student from the anatomy lectures of Alexander Monroe II at Edinburgh. This places the date at about 1780. I quote from these notes as they appear in Volume 1, pages 53-54, of the manuscript: "formerly the Book I now show you, the work of Vesalius was universally recommended, & you observe that the figures are very elegant, yet altho' considering the time in which it was composed this work is praise worthy, he has shown too much action of the muscles, whereby he has misled many of the painters, in some places too the parts of other animals have been substituted instead of the human body. I would therefore recommend in place of Vesalius, the more correct & useful work of his Cotemporary (*sic*) Eustachius, & you see here his Original Tables, which I said were in danger of being lost, & were only discovered by the care of Lancisius. At first sight we are convinced that the Tables of Eustachius in point of execution and elegance are infinitely inferior to those of Vesalius, nor can they well fail to be so, from the manner of their Construction, first he places before the Painter a Skeleton, then he makes a Dissection & he instructs the painter, attends himself to the Connexion of the several muscles, & instructs the Painter how he should transfer the muscles upon the Skeleton, without drawing the parts exactly as they lay before them, perhaps to conceal this art we find another fault in the System of Eustachius that instead of beginning with the structure of the Bases, he ends with it, that, in studying his Tables we ought to reverse his order, yet such attention is given to the true situation of the several organs, & many of the more minute Blood vessels & nerves are traced with such Care that anatomists have agreed to prefer these Tables even to the more modern works of the same kind, . . ."

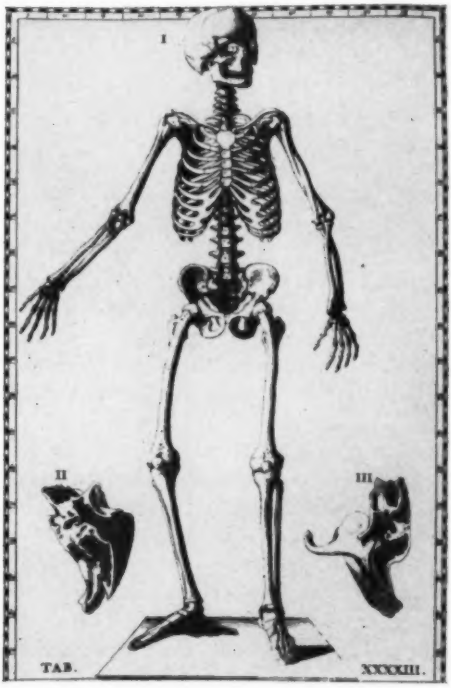



Figure 4

On Plate VII (Fig. 2) are engraved a figure of a section of the kidney of the dog, a figure of the ossicles of the dog correctly articulated and delineated with the tensor tympani muscle (this muscle having been first observed and described by Eustachius) and a similar figure of the ossicles and muscle of man. None of these figures is indicated by figure numbers. This plate is one of the eight mentioned above all of which appear in Eustachius' Opuscula Anatomica,[7] published in 1564 of which the Epistola de Auditus Organis forms a section and which was dated October, 1562, and which apparently were not engraved by de Musi.

These figures of the ossicles and muscle reappear (Fig. 3) in their proper setting in the group of figures of muscles of the face and throat on Plate XXXXI of the Tabulae Anatomicae where they are numbered X and IX. Note that these figures are numbered consecutively from right to left, whereas all other figures on this plate are numbered from left to right in accordance with usual custom.

Most authorities feel that Eustachius shares with Ingrassia a claim to priority in the description of the stapes, each having described it independently and approximately simultaneously.

In the Epistola (1562) Eustachius gives a complete and quite accurate description of the cochlea describing it as consisting of two or three turns. The description recognized today is two and three-quarters turn. However no illustration of the cochlea appears in the Epistola and he fails to make any mention of the semicircular canals.

Notwithstanding the above facts, on Plate XXXXIII of the Tabulae engraved ten years earlier, there are two figures of sections of the temporal bone labeled II and III (Fig. 4). The one labeled II shows the subarcuate fossa and sections of two of the semicircular canals. On Plate XXXXIIII (Fig. 5) again appear two figures of the temporal bone labeled II and III. These show the topographical locations of the canals on the surface of the temporal bone. In the 1714 Lancisi edition of the Tabulae these are called the serpentine or spiral labyrinthine duct in II, and in III they are called the continuation of the serpentine duct. In the 1744 (or first) Albinus edition they are called semicircular canals. On Plate XXXXV (Fig. 6) appears a section of the temporal bone labeled II. This shows in amazing clarity a cross section of the cochlea showing two turns and a vertico-diagonal section of at least two of the semicircular canals.

The figure labeled I in each of these three plates shows full front, back and side views of the complete human skeleton respectfully. Quite obviously these were intended to be full page figures as are all of the complete bodied muscle men.

Plate XXXXVI (Fig. 7) showing the complete and disarticulated skull is quite filled. But on this plate the figures labeled X, and XV and XVII except for minor variations of the suture lines, are the same. At least two of them might well have been "fillers" (XV not being

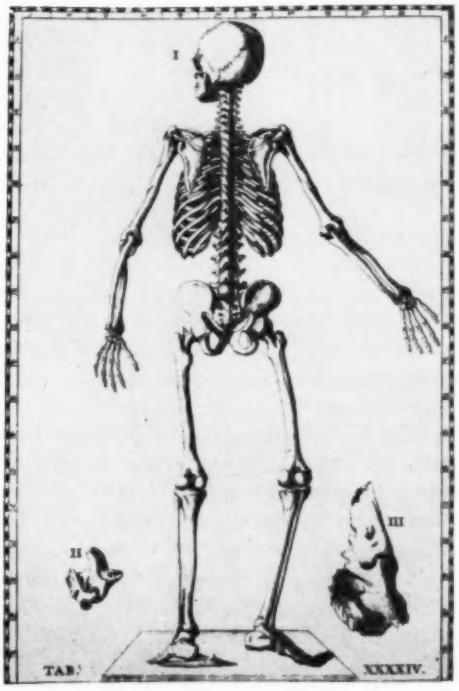



Figure 5

mentioned by Lancisci and XVII not being mentioned by Albinus) that could have contained the five figures of the temporal bone on Plates XXXXIII, XXXXIIII and XXXXV. These, please remember, were engraved in 1552, ten years before the Epistola de Auditus Organis was written and twelve years before it was published in which no mention of the semicircular canals was made.

The figures of the ossicles and muscles appearing on Plate VII of the Tabulae are authentic. But we are now forced to question whether the otologic figures on Plates XXXXI, XXXXIII, XXXXIIII and XXXXV appeared there when the plates were engraved originally. I

cannot avoid the feeling in view of the patent evidence presented that they were added at a later date, probably at the direction of Lancisi or by the publishers of the 1714 edition.

So much for the medical hoax.

And now we come to the second episode in the odyssey. This, too, is found in the Epistola. After Eustachius completed his description of the cochlea he wrote these lines on pages 160 and 161:

"Hanc miram opificis nostri industrium, primum innuisse Empedoclem suspicor: quum, ut testis est Galenus in libro de historia philosophica, auditum impulsione fieri docuit qui cochleae simile intra aurem tintinnabuli instar suspensum percutit atque pulsat. Cui etiam Aristoteles assentire videtur, asserens primo de natura animalium undecimo, partem interiorem auris forma anfractui cochleae desinere in os, quod auriculam plane imitatur."[8] (This marvelous work of our [laboratory] worker I suspect Empedocles hinted at first of all; when as Galen is witness in his book on philosophic history, he showed that hearing takes place by an impulse of air (spiritus) which strikes and makes pulsate something similar to a snail suspended like a bell within the ear. With him Aristotle seems to agree, mentioning it in the first book of the Natura Animalium, paragraph eleven, that the inner part of the ear is similar in shape to the curves of a snail ending in a bone in which the little ear plainly is imitated.)

And so we trace the story of the cochlea, by the honesty and frankness of Eustachius, through Galen and Aristotle to Empedocles in the fifth century, B.C. The only other reference available to me, attributing knowledge of the internal ear to Empedocles, is by Sarton in his History of Science, "He recognized the labyrinth of the ear," probably not an accurate statement as Empedocles mentions only the cochlea.[9]

After the recognition of its anatomy, the evolution of the concept of the internal ear as an organ of hearing proceeded rapidly, Cotunnius[10] noting the fluid present and Scarpa[11] the membranous labyrinth. All investigators and clinicians regarded the semicircular canals as quite important factors in the process of *hearing*.

Duvernay in 1683[12] recognized the structure of the cochlea as being applicable to the reception of sound. The semicircular canals

Figure 6

with their ampullated ends he likened to trumpets with their sonorous characteristics responding in common with the cochlea. Curtis in 1817[13] regarded the canals as reflectors which intensify the sounds as do the vaults of the roof of a church. Pilcher in 1838 who was awarded the Fothergillian Medal by the Medical Society of London for the excellence of his Treatise on the Structure, Economy and Diseases of the Ear[14] therein regarded the cochlea as a receptor of coarse sounds and the canals because of their curvature as perceptors of finer sounds. Bryan who wrote the first American text book on Otology in 1851[15] held the labyrinth to be the essential and the cochlea to be the accessory organ of hearing. Although Darwin in 1801[16] described giddiness following turning, he in no way associated the ear with this phenomenon.

However in 1828 Flourens[17] by section of individual canals in pigeons and later that year[18] confirming his findings in mammals noted head *movement* in the plane of the operated canal and suggested that the VIII nerve is divided into cochlear and vestibular portions. This is the first recognized connection of the ear with motion.

Ménière in 1861[19] clinically established the internal ear as being a source of episodic vertigo.

The problem of tinnitus has long puzzled otologists. Its detailed story is too long and too involved to come within the purview of this limited discussion. It is only within the past few years that a possible psychosomatic basis has been recognized. In 1904 Bryant[20] closely approached this subject in speaking of "central tinnitus in nervous excited individuals."

In May 1950 Goodhill[21] speaks of the "psychosomatic loading factor" and credits an earlier work of E. P. Fowler, Sr. for original mention of it. In September 1950 E. P. Fowler, Sr. and E. P. Fowler, Jr.[22] for the first time in modern medicine designated emotional disturbances as a basic factor, and not as an overlay, in tinnitus. Here they state: "Profound changes in both man and beast occur from *fear*, rage. . . ." These changes they aver are mediated by the neuro-vascular mechanism. Please note that of the emotional disturbances they mention fear before all others.

Thus we may conclude that the ear first was associated with motion experimentally in 1828 and clinically in 1861, and a possible psychosomatic basis for tinnitus was first postulated within the past decade. This would seem to bring our story to a neat and satisfactory conclusion.

But you will recall that I spoke of three episodes of interest on this journey. The third appears long years before any of the recorded events concerning motion and tinnitus that I have just recounted. And so for a brief moment let us take a long step backward in the printed records of medicine.

The Medical School of Salerno apparently was the first "lay" institution in the "midst of purely clerical foundations" to come into existence. "It lifted medicine in the eleventh and twelfth centuries

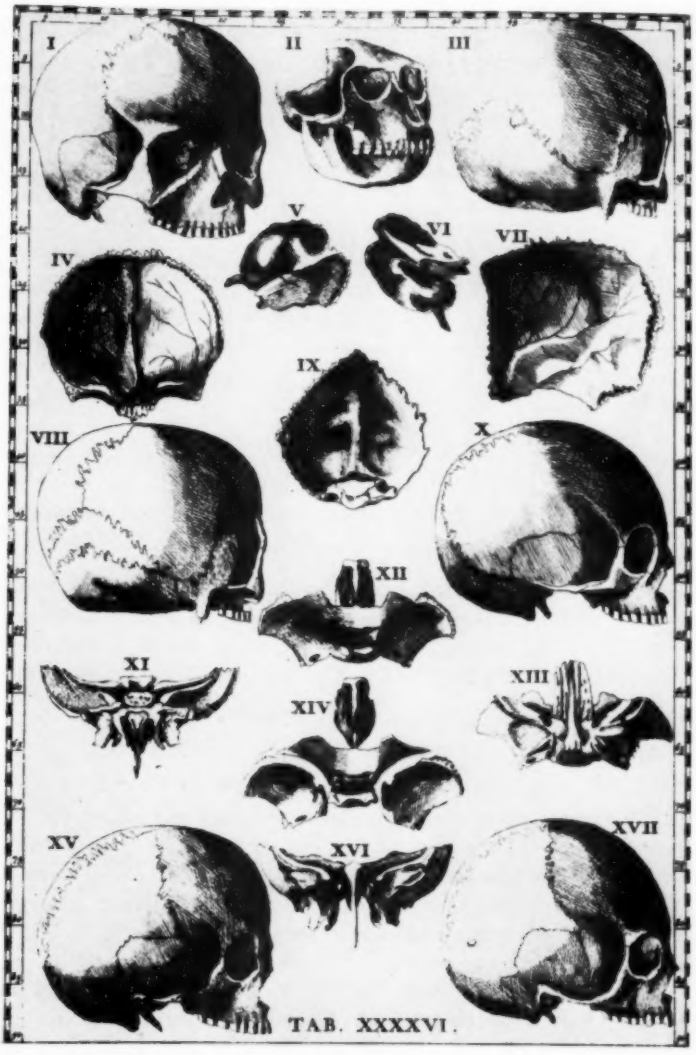

I
II
III
V
VI
VII
IV
IX
VIII
X
XII
XI
XIII
XIV
XV
XVI
XVII
TAB. XXXXVI.

Figure 7

to a much higher level . . . diseases were studied first hand in a straightforward, spontaneous engaging manner."[23] Among the works emanating from Salerno is the Regimen Sanitatis Salernitanum. It is a poem in double rhymed hexameters giving causes of diseases and rules of health and was composed by an unknown author (or authors) during the years 1230-1300. The first printed Latin edition is undated. But it is known that several such undated editions were printed about 1480-1484. It is not known with certainty which of these is the first edition.

In 1948 I purchased from Mr. Harold Graves, then with Brentano's of Chicago and now with Scribner's of New York, a copy printed in Frankfort in 1559.[24] I purchased it simply because it contained a woodcut of the external ear which signalled to me that something of interest to an otologist was present. I was right. That something was startling indeed. It was the following verse:

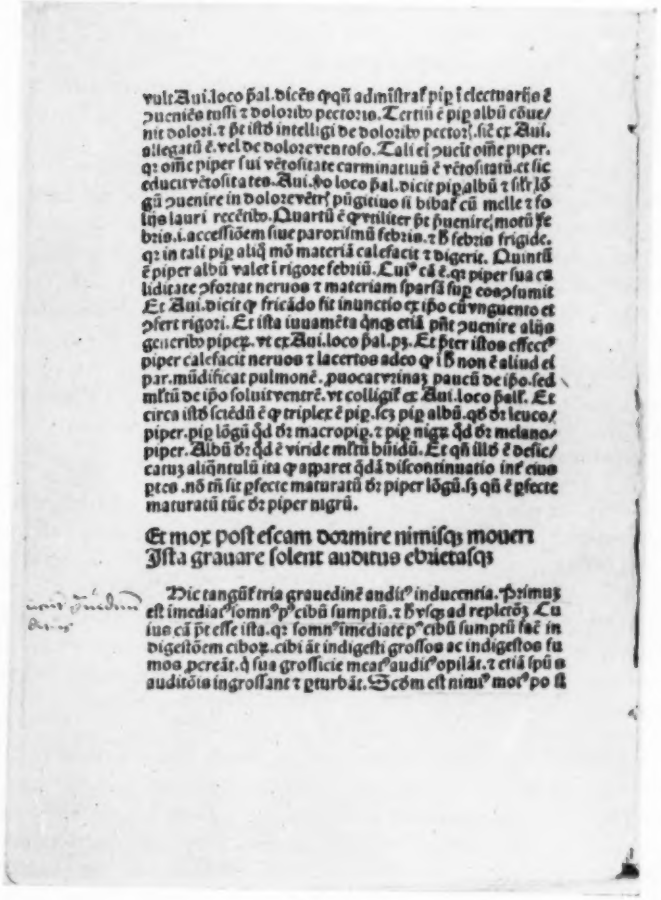
> Et mox post escam dormire, nimisque moveri
> Ista Gravare solent auditus, ebrietasque.
> (And to sleep immediately after eating, and to move violently,
> And drunkenness, these usually cause dullness of hearing.)

Here was a voice speaking from the thirteenth century connecting the ear with violent motion, whereas documented medical history tells us, as I have just related, that such a concept is just a century old. And I was even more surprised by the verse that follows immediately:

> Motus, longa fames, vomitus, percusio, casus,
> Ebrietas, frigus, tinnitum causat in aure.
> (Motion, long fasting, vomiting, a blow, a fall,
> Drunkenness, chilling cause ringing in the ear.)

Here again the ear is associated with motion. This time it is tinnitus, one of the symptoms of Ménière's syndrome of episodic vertigo which is truly a sensation of motion.

But more was to follow. In 1953 I purchased another and much earlier copy of the book from Mr. Otto Ranschburg of Lathrop Harper's of New York. It is dated 1491.[25] The first of the two verses in question as can be seen from illustration of the text (Fig. 8) agrees with the text of the 1559 edition. But I felt sure that a misprint had



vult Aui. loco pal. dicēs qqñ administrat pip̄ i electuarijo ē
ꝓueniēs tussi ꝛ doloribꝫ pectoris. Tertiū ē pip albū cōue/
nit doloꝛi. ꝛ pt istō intelligi de doloribꝫ pectoꝛis. sic̄ ex Aui.
allegatū ē. vel de doloꝛe ventroso. Tali ei ꝓuenit oīe piper.
qz oīe piper sui vētositate carminatiuū ē vētositatū. et lic
educit vētosita tes. Aui. ho loco pal. dicit pip albū ꝛ sitr lō
gū ꝓuenire in doloꝛe vētꝛis pūgitiuo si bibat cū melle ꝛ fo
lijs lauri recētibꝫ. Quartū ē q̄rnliter pt ꝓuenire, morū fe
brīs. i. accessiōem siue paroxismū febrīs. ꝛ b̄ febris frigide.
qz in tali pip aliq̄ mō materiā calefacit ꝛ digerit. Quintū
ē piper albū valet i rigoꝛe febriū. Cui⁹ cā ē. qz piper sua ca
liditate ꝓfoꝛtat neruos ꝛ materiam sparsā fugꝫ coꝛsumit
Et Aui. dicit q̄ fricādo fit inunctio ex ipo cū vnguento et
ꝓfert rigoꝛi. Et ista iuuamēta ānq̄ etiā pñt ꝓuenire aliīs
generibꝫ pipeꝛ. vt ex Aui. loco pal. ps. Et ꝑter istos effect⁹
piper calefacit neruos ꝛ lacertos adeo q̄ i b̄ non ē aliud ei
par. mūdificat pulmonē. paucā vrinaꝫ paucū de ipo. sed
mltū de ipo soluit ventrē. vt colligit ex Aui. loco pall. Et
circa istō sciēdū ē q̄ triplex ē pip. sc̄z pip albū. qđ oꝛ leuco/
piper. pip lōgū qđ oꝛ macropip. ꝛ pip nigꝫ qđ oꝛ melano/
piper. Albū oꝛ qđ ē viride mltū biliōū. Et qñ illō ē desic/
caruꝫ aliīntulū ita q̄ apparet qđā discontinuatio int̄ eius
ptes. nō tñ sit pfecte maturatū oꝛ piper lōgū. sꝫ qñ ē pfecte
maturatū tūc oꝛ piper nigrū.

**Et mox post escam dormire nimisq̄z mouerī**
**Ista grauare solent auditus ebrietasq̄z**

Dic tangūt tria grauedinē audit⁹ inducentia. Primuꝫ
est imediat⁹ somn⁹ p⁹ cibū sumptū. ꝛ b̄ vsq̄z ad repletiōz. Cu
ius cā pt esse ista. qz somn⁹ imediate p⁹ cibū sumptū fac̄ in
digestiōem ciboꝝ. cibi ār indigesti grossos ac indigestos fu
mos. pcreār. q̄ sua grossicie meat⁹ audit⁹ opilār. ꝛ etiā spū a
auditōꝛis ingrossant ꝛ turbār. Scōm est nimi⁹ mot⁹ po st

Figure 8

occurred in the opening line of the second verse, for here the verse opens with the word "Metus" (Fig. 9) rather than "Motus." Later I noticed the hand written gloss "Metu" in the margin connected with the hand drawn line underlying the sentence in the commentary, "Quorum primum est metus et secundum alios motus" (Of which the first is fear and according to others it is motion). This text is identical with that of one of the earliest Latin printings of 1480-1484[26] which I have most recently purchased from Mr. Ranschburg.

Here indeed is a "gem of purest ray serene" borne by "dark unfathom'd caves of ocean." We who have only yesterday recognized that fear with its associates, anxiety and tension, may cause tinnitus find ourselves antedated by an observer six full centuries ago. And further we find in the underlined commentary that this view was perhaps a little too far advanced for its time and that the concept of motion was more acceptable than that of fear. In only one later edition available to me have I found that the word fear (metus) occurs again. It is changed to motion. This then is added evidence that at that time the ear was commonly considered in some clinical way to be connected with motion.

It is amazing that the significance of this should have escaped the attention of observers far more astute than the writer of this paper. Even Politzer after quoting portions of these verses in his History of Otology[27] writes, "Von dieser traurigen Epoche in der Geschichte der Medizin wenden wir uns den bedeutendsten Repraesentanten der Schulen von Salerno und Montpellier zu." ("From these dreary epochs in the history of medicine we turn to the most significant representatives of the Schools of Salerno and Montpellier.")

Possibly the key to understanding why these noteworthy clinical observations were consigned to limbo may be found in the commentaries ascribed to Arnoldus de Villanova. Here in our own English translation is considerable medical nonsense in the honest effort of a mind to integrate a view in advance of its time with the background of the so-called knowledge of its time.

> And to sleep immediately after eating, violent motion and drunkenness
> These cause difficulties [heaviness] of hearing.
> Here three causes induce difficulties of hearing.
> The first is sleeping immediately after eating food to repletion.

cibū sumptū. qz talis etiā impedit digestōz z clausionē debitā orificij stōachi. Aliq̄ tñ text⁹ loco nimis hāt minus. et tūc sensus ē q⁹ null⁹ mor⁹ post cibū sūptū etiā ḡuat auditū. Cui⁹ rō ē. qz tūc orificiū stōachi nō ita facile claudit sicut ꝑ paucā deambulatōz. q̄ cibi descēdūt ad fūdū stōachi ℨ stōacho nō existēte clauso fumi ml'ti ascēdūt ad caput grauātes auditū. Tertiū ē ebrietas. qz ex ebrietate pcreant fumi ml'ti z vapores q̄ ascēdūt ad caput z ad organū audit⁹. spūs et⁹ turbātes z auditū gr̄ātes. z nō solū ebrietas inducit nocumentū auditui. ℨ etiā risus. Et offitio sensitiu ꝑter eandē cām. vt etiā ꝓpter dictū ē. Aui. ſo. iiij. in. c. ij. de ꝓseruatiōe sanitat⁹ auris etiā dat tria nocēcia auribꝰ. z dicit. et ex eis q̄dē q̄ nocēt auri z relictio sensitiu sūt fastidiū z repletio z ꝓpter somn⁹ sup repletōnem. Et ē sciendū q⁹ aliq̄ text⁹ adhuc hāt istū versū ꝓtinentē adhuc alia inducēcia graue dinē audit⁹. z est iste. Balnea sol vomit⁹ affert repletio clamor. qz ista inducūt etiā grauedinē audit⁹. maxime tamen tinnitū. q⁹ dicit Aui. iiij. in. c. de cura tinnitus Oportet vt omnes iste vitent solem z balneū laboriosum z vomitum et clamorē z repletōem.

**Metus. lōga fames. vomit⁹. percussio. casus. ebuetas. frigus. tinnitum causat in aure.**

Hic cāgāt sepē inducēcia tinnitū i aure. i. sonum quem hō videt audire extern⁹. Quoz ꝓmū ē met⁹. et ſm alios motus. Causa ē de metu. qz in metu spūs z būores monētur ad interiora. s. ꝓpter cor subito. et q̄ motu facile mor⁹ generat vētositatē. q̄ penetrādo ad organū audit⁹ tinnitū causat. De motu etiā p̄. qz ex motu corporali etiā ꝓmouēt būores z spūs et q̄ ꝓmotōe etiā generat vētositas facile q̄ veniens ad aurem tinnitū causat. qz tinnit⁹ causat ꝗcūq; ꝓpter aliquā ꝓmotōem vapor aut vētositat⁹ circa organū audit⁹ cōmouentē sicē ꝓnaturē i organo audit⁹ existētē. Sciēm ē lōga fames.

b 3

Figure 9

Whose basis is that sleeping immediately after taking food produces indigestion of the food, either gross indigestion or disturbance of the fumes which it generates, which massively blocks the auditory meatus and surely the spirit of the hearer is heavier and disturbed.

Secondly is excessive motion after ingestion of food because this also impedes digestion and accounts for closure of the mouth of the stomach. However anything in the pattern of excessive motion at that time decreases at the same time perceptiveness as though [to] nothing. Motion after ingestion of food certainly disturbs hearing. The reason for this is that then the mouth of the stomach is not active; it is crippled by the smallness of the passage by which the foods descend to the fundus of the stomach. At such times there does not exist in the stomach a bar to the many fumes ascending to the head impairing the hearing.

The third is drunkenness for from inebriety there are produced many fumes and vapors which ascend to the head and to the organ of hearing. These spirits are disturbing and depress the hearing. And drunkenness not only produces harm to the hearing but also to vision and to all the senses following the same route (of) cause in the manner certainly first mentioned by Avicenna, Volume 4, in Chapter II concerning conservation of the health of the ear definitely presenting three means of damage to the ear and stating that it is from these by which the ear and the remaining senses are harmed—loathing of food, over-eating and particularly sleeping after eating.

And [it is] according to other texts that have this verse containing still other means of inducing difficulties of hearing, and it is this: Bathing, the sun, vomiting, over-eating, noise, each of these surely induces difficulties of hearing [and] in the most exaggerated cases tinnitus aurium. Avicenna speaks [of this] in Volume 4 in the chapter concerning the treatment of tinnitus: It should be recommended that all of these ought to be avoided—the sun, excessive bathing and vomiting and noise and over-eating. (For the medieval Latin text, see Figs. 8 and 9.)

> Fear, long fasting, vomiting, blows, falls,
> Drunkenness, chilling cause ringing in the ears.

Here are discussed seven causes inducing ringing in the ears which seem to be heard by a person externally. Of these the first is fear

Et trõnẽ subiũgit Auí. liũ. in. c. lx. dicẽs. ꝛ illis ẽ ꝓpagitatõ nẽ cadentẽ i hũoꝛibꝰ sparsis i coꝛpe ꝯdescẽdo i ipo. Et cuꝫ nõ inuenit naꝛa cibũ aliquẽ ꝓuertit ad eos. ꝛ soluit ipsos ꝛ mouet eos. Tertiũ ẽ vomitꝰ. qꝫ i vomitu ꝯ est molꝫ laboꝛiosus mouẽt maꝛie hũoꝛes ad caput. In signũ cuꝫ oculos ꝛ faciẽ videmꝰ fieri rubeos. ꝛ vilus fieri nocumẽtũ. Et sic etiã facile mouent in vomitu vapoꝛes ꝛ vẽtositates ad oꝛganũ audituꝰ. Quaꝛtũ ẽ pcussio spe in capite ꝛ maxie i aure. Cuꝰ cã ẽ. qꝫ ex tali etiã accidit vehemẽs ꝓmotio aeꝛ cõnaꝛalis in oꝛgano auditꝰ exist̃s. qꝫ naꝛa aliꝫ mẽbꝛo ieso i mediate mittit ad ipm spũ ꝛ sãguinẽ ꝙ sunt instꝛa naꝛe. ex ꝙbꝰ tũc accidit i aure ꝓmotio. Quintũ ẽ casus. ꝛ maxie supꝛa caput. ꝓpt eandẽ cãm ꝙ dicta ẽ de pcussiõe. ꝛ etiã ex casu ꝙcũqꝫ vehemẽs fit ꝓmotio hũoꝛ in coꝛpe. Sextum est ebꝛietas. cuꝰ cã ẽ. qꝫ in ebꝛietate caput replet fumis ꝛ vapoꝛibꝰ. ex ꝙbꝰ ad oꝛganũ auditꝰ vehementiꝰ facile cõmouet aeꝛ ꝓnaꝛalis i oꝛgano auditꝰ exist̃s. Septimũ ẽ frigꝰ. ex foꝛti cũ frigoꝛe debilitat oꝛganũ. aꝛe ex leui cã facile patit vel ꝓtingit tinnitꝰ ex foꝛti frigoꝛe. qꝫ foꝛte frigꝰ causat vẽtositates. Et nõ solũ existio causis ꝓtingit tinnitꝰ auriũ. imo ex pluꝛibꝰ aliis sicut ex vẽtositate i capite generata ꝛ i ipo mota. aut ex sonitu saniei ꝙ generat foꝛtasse i ipa. ꝛ ex feruoꝛe puꝛis i pꝛibꝰ eꝰ aut ex motu vẽtositatis accidẽs multotiens in meatibꝰ eꝰ. sic fit in febꝛibꝰ aut ex repletiõe superflua i coꝛpoꝛe ꝓpe in capite. aut ex mateꝛia viscosa resoluta i paucã ventositatem. aut ex medicinis. quaꝝ ꝓpꝛietas est vt retineant hũoꝛes et ventositates in tẽpoꝛibꝰ cerebꝛi. vt colligit ab Auicen. loco ꝓalle.

Balnea vina venus ventus piper allea fumus
Pdori cum cepis lens fletus faba senepis
Sol coitus ignis labor ictus acumia puluis
Ista nocent oculis sed vigilare magis.

Figure 10

and [but] according to others it is motion. The cause is from fear because in fear the spirits and humors are moved toward the interior, namely [that is], against the heart with violence from which action is generated a labile movement of the flatulence which penetrating to the organ of hearing causes ringing. Concerning this motion it surely is clear that from the motion of the body (which) surely agitates the humors and spirits from which commotion are generated labile flatulence which, reaching the ear causes tinnitus: which tinnitus is caused following some commotion of the air which naturally exists in the organ of hearing.

Second is long fasting and the reason [for this] is proposed by Avicenna Book 4 in chapter 9 [in which] he states "and the decrease is followed by agitation [and] fall in the humors which are sparsely dispersed in the body being quiescent in it, And which condition is not found in the properties of food or anything converted to them by dissolving it or moving them.

The third is vomiting because in vomiting, which is a labored motion, the humors are moved to the greatest degree toward the head. in sign of which the eyes and face are seen to be red and the vision is noted to become impaired. And thus surely in vomiting the vapors and humors are moved with facility to the organ of hearing.

Fourth is a blow on the calvarium [of the head] and especially on the ear. Of which the cause is that from such categories comes violent commotion of the air coming naturally into the organ [and] existing there. Which because nature, when some portion of the body is damaged it immediately sends to it spirits and blood which are liberated naturally when then increase the commotion in the ear.

The fifth is falls, most especially on the head, whose causes of which follow the same route as discussed concerning blows and which surely follow blows whenever there is violent commotion in the humors of the body.

The sixth is drunkenness whose cause is that in drunkenness the head is filled with fumes and vapors which are moved violently and with facility as the air existing naturally in the organ of hearing is agitated.

The seventh is marked chilling because cold debilitates the organ so that it is opened even by slight causes so that tinnitus may enter [appear?] from marked chilling. Such marked cold causes flatulence, [wind currents?].

And not alone from these causes may tinnitus aurium occur: but even more from many others. As for example from winds in the head which are generated and move strongly there. Or from the sound of the blood which probably develops within and entirely from agitation: [and] in part surely from movement of the flatulence occurring very often in the meatus, as happens for example in fever or from an overflowing repletion [of the blood] in the body, particularly in the head. Also from viscid material loosed in scanty flatulence; also from medicine whose properties it is to retain humors and flatulence in the temporal brain as discussed by Avicenna in the previous [cited] place. (See Figs. 9 and 10.)

In drawing a cloak of medical charity about these commentaries let us bear in mind that many worthy clinical observations of our time have been damned by commentators whose minds are unable to accept a fact for which they can supply no supporting theory, or even worse who supply theories so weighted with absurdities that the buoyancy of the fact cannot support them and they all sink. And now I hear a still, small voice asking, "Doctor, you who are castigating so mercilessly these commentaries of old, are you sure that Arnoldus de Villanova was entirely wrong? Are you sure that he is not speaking to you in words whose deeper meaning you do not grasp?* May I ever so gently remind you, Doctor, that the fact that the 'Heathen Chinee' physicians for four thousand years were relieving asthma and nasal congestion with a plant called Ma Huang was ignored by Western physicians until ephedrine was isolated from the plant. This made it modern and 'scientific' and therefore acceptable."

Much that we have not yet divined has gone before us and remains to be rediscoverd. Truly the Preacher was right when he wrote in Holy Writ:

"*Quid est quod fuit: Ipsum quod futurum est.* That which is, has been: It is the same that will be. *Quid est quod factum est: Ipsum*

* Quite recently in discussing with Professor Gosta Dohlman the pressures exerted upon the intralabyrinthine fluids he made the casual remark that these fluids were slightly compressible *because of the gases dissolved in them.*

*quod faciendum est.* That which has been done, It is the same that will be done. *Nihil sub sole novum.* Nothing under the sun is new. *Nec valet quisquam dicere: Ecce hoc recens est.* If there is anything of which it may be said: Behold this is of recent time. *Jam enim processit in seculis: qui fuerunt ante nos.* It has already gone forth in times which were before us."

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Grateful acknowledgement is made to A. J. Cronin, Ph.D., Professor of Latin at Southern Methodist University for his redaction of my amateurish translation of the Latin passages from the Regimen Sanitatis and the Opuscula Anatomica of Eustachius, to Miss Gertrude Annan and Mrs. Alice Weaver of the Library of the New York Academy of Medicine and to Miss Salmonsen of the John Crerar Library of Chicago for their assistance in locating needed source material.

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LVII

# AURAL EMBRYOPATHIES

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Edward Cock, in 1838, published in Guy's Hospital Reports (Vol. 7, pp. 289-307, Oct.) "A Contribution to the Pathology of Congenital Deafness." He complained that ". . . the pathology . . . of diseases of the ear has, until lately, been almost wholly neglected"—in contrast with "every other department." As a personal contribution he offered an investigation, by macroscopic dissection, of seven pairs of ears, originating from an Asylum for Deaf and Dumb. He described malformations in the inner ear, and tried to bring them into relation with congenital deafness as known by clinical experience. In the following period many followed his example, often taking advantage of similar material. In this way the chapter on malformations grows to become a very impressive system. Functional defects were readily correlated with irregularities of the development from extensive deformities to minute displacements of the papilla of Corti on the basilar membrane.

But Cock already felt that this path to progress was not entirely satisfactory. He wrote: ". . . there must be some other defect, either organic or functional, the demonstration or explanation of which has, as yet, eluded our research." He can hardly be reproached for leaving the task uncompleted; a full century was to pass before, in 1941 a rubella epidemic in Australia opened a wide door for new conceptions.

Bamatter, in 1946, was the first to apply the term "embryopathy" to the non-genetic, developmental disturbance and disease of the future child. A number of previous, scattered observations were claimed as belonging to this domain.

Following the example of the general pathologist in studying the offspring in cases of adequately observed and followed maternal dis-

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ease, we started with rubella, proceeded to fetal erythroblastosis, poliomyelitis, toxoplasmosis, and secured, whenever possible, fetal, perinatal and early postnatal specimens. Related material, however, turned out to be so rare that we tried to procure a basis for comparison by working with such well known conditions as birth trauma, syphilis, diabetes, and nephritis. After wandering, so to speak, among the foothills, we turned for a safe background to the range of high mountains. But here, too, and quite unexpectedly, a scarcity of fetal and perinatal observations was encountered, in spite of a search back over many decades.

Animal experimentation with lesions such as poisoning, radiation, anoxia served to fill in some of the numerous gaps, but this approach will be here disregarded, to restrict the demonstration to findings in humans. In this way, several pitfalls will be avoided, such as interference by spontaneous pathology in experimental animals and the always dubious applicability of results to human conditions.

Thirty-eight pairs of ears were examined in sectional series. Twelve pairs originated from the period around the boundary of the first and second gestational trimester; the remaining 26 belonged to the perinatal period, including prematures and cases with macroscopically observable deformities.

To arrive at a synthesis we shall proceed along the anatomical sequence of elements which constitute the peripheral organ of hearing. The external meatus and the tympanic membrane will be omitted although they showed, in instances, changes which could easily lead to cholesteatoma formation later.

Of first importance were signs as found in the mesenchyme, the main source of definitive formations. Rearrangement, by buds with origin in the submucosa, was well on its way, be it organization or reabsorption. The main cellular elements were present in variable proportions, while foci of dense cellular infiltration were spotted in many locations, as in rare remnants of mesenchyme in the cochlear duct. Fibrous organization surrounded, at a very early stage, the incudomalleolar articulation. Hyaline masses were formed, e.g., in the window niches, and vacuoles filled by transudate or fibrous content. Most conspicuous were the vascular phenomena. Cuffing was seen around vessels, the latter in solitary course or in conglomerates.

In the perilabyrinthine pneumatic cells blood lakes formed in the mesenchyme, and many cushions in the window niches were characterized by a high degree of vascularization. Cells were seen pouring from the newly differentiated mucoperiosteum to be caught in the fibrous meshes inside mesenchymal vacuoles, a phenomenon not observed hitherto.

The course of the transformation of the myxomatous tissue into loose fibrillar tissue and later into the permanent mucoperiosteum, in combination with inflammatory products, has to be followed with greatest attention.

The *ossicles,* even in our youngest specimens, were fully outlined in cartilage, as expected in normal development. Ligaments were outlined in the mesenchymal mass as condensations. Ossicular malformations were observed in several instances, such as absence of one stapedial crus or deficient continuity between incus and stapes. But, from the viewpoint of this presentation, the inflammatory phenomena that lead to organization products in the window niches claim first importance.

As mentioned, vascular changes as engorgement and extravasates were conspicuous in the mesenchyme of the middle ear; their real significance became more obvious in the inner ear.

The endolymphatic spaces of the vestibular and the cochlear portions of the *inner ear* very early became free of mesenchyme, which remained much longer in the perilymphatic portions. Consequently, phenomena like engorgement, extravasation, cellular infiltration originated in the perilymph. Edema was sometimes the next step, with compression of the endolymphatic tube.

Within the endolymphatic tube serious consequences threatened the *sensory end organs.* Two characteristic lesions will be described.

Hemorrhage can hit the ampullar section of the *semicircular canals* through a leak in the endolymph-perilymph septum, usually near the richly vascularized section near the base of one of the cristae. The latter proved to be remarkably resistant, preserving an intact structure including the hair cells with hairs. On the other hand, the cupula showed extreme vulnerability toward blood extravasates

reaching its surface; every erythrocyte seemed to bite into the substance of the cupula. A characteristic picture was a cupula with one edge intact, and the other deeply excavated wherever contact with an extravasate was established. The consequences of deprivation of a crista of its cupula are obvious, and nothing is known about a possible regeneration of the latter, e.g., after reabsorption of the surrounding extravasate.

In the *cochlea* the threat of specific damage to the end organ came from the direction of the vascular stria. The latter may show calcifications, but more important were the engorged vessels. Those running along the surface ruptured, with the consequence that extravasate filled the cochlear duct. The organ of Corti was in all cases well formed in accord with the respective developmental stage, and was inundated. While the extravasate may be reabsorbed, the consequences of even a temporary filling of the cochlear duct can hardly be calculated.

Engorgement and extravasation within the vascular apparatus of the modiolus and, finally, peri- and endoneural extravasation in the VIII nerve are too obvious in their consequences to need discussion at this point.

The manifold lesions in the peripheral organ are put into adequate perspective when scrutinized against the severe changes in the organs of the near vicinity, especially the brain and the eye.

## SUMMARY

In numerous instances of embryopathy (intrauterine disease) the sensory end organs remained conspicuously intact even amid severe lesions in the adjacent regions. In these cases functional loss must originate from destructions in the central pathways.

Damage when localized in the peripheral organ can usually be traced to a vascular lesion. The consequences of debility, fragility of vessels, become manifest at any period of strain, in intrauterine, perinatal and extrauterine life.

Embryopathies, of viral, bacterial, protozoan, metabolic or any other origin, represent an immense field; light is shed so far merely

on some widely scattered points of its expanse. It is hardly possible to think of a more stringent duty for aural pathology than to establish a comprehensive picture of the danger in embryopathies, to which the hearing capacity in the offspring becomes exposed.

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LVIII

# COCHLEAR BLOOD FLOW DURING HYPOTHERMIA

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Sudden derangements of labyrinth function seen in the clinic are often considered to be the result of powerful vasomotor responses of the labyrinth blood vessels. To date our experimental studies[1] on these vessels in the cat and guinea pig have failed to reveal this vasomotor phenomenon. On the contrary, the behavior of the cochlear vessels were found to resemble that of cerebral vessels where vasomotor stability is one of the outstanding characteristics. The present study was designed to obtain further information on this point. We rapidly reduced the body temperature of animals to a state where fibrillation and even cardiac arrest occurred in an attempt to produce vasoconstriction of cochlear vessels. During cooling, motion pictures were taken of cochlear blood flow. Although a great deal of data has been obtained on blood flow in various organs during hypothermia[2] only a limited amount of information has been based on direct observation of the terminal vascular bed and none has been carried out on the terminal vessels of the cochlea.

The experiment was carried out on 20 young (270 gm) guinea pigs under dial and urethane anesthesia. Ten animals were subjected

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to hypothermia and ten were not, thereby serving as a control group. Both self respired and artificially respired animals were studied. Heparin was used in all and crurare in those placed on the respirator. The surgical procedure and apparatus for recording cochlear blood flow has been described in earlier reports.[3] The apical end of the cochlea is fenestrated and transilluminated by the solid quartz rod technique and motion pictures of the blood flow at 16 to 42 frames per second are taken through a microscope. By these means, vessels of the stria vascularis and the spiral ligament vessels were exposed to direct inspection at magnifications from 96 to 390 x. In addition, the mean blood pressure at the common carotid artery, heart rate, electrocardiogram and rectal temperature were measured. Records were taken at five minute intervals before and throughout the period of cooling. Cooling was effected by covering the body with ice and proceeded at about .2° C per minute. The region between 30 and 20° C was particularly examined although cooling was at times continued to complete cessation of heart heat and circulation (about 16° C). The diameter of the vessels was measured on a projection screen by comparison with a micrometer scale similarly photographed. The rate of blood flow was measured by recording the number of frames required for movement of white blood cells through a given segment of a vessel. This method was considered feasible because a uniform movement of these elements along the vessel has been seen consistently in this field during many previous observations. Occasional clumps of cells that did not move uniformly were not used for measurement. White blood cell counts were made, in a number of instances, before and after surgery to determine whether the operation appreciably changed the number of white cells in the circulating system. Aside from recording the behavior of cochlear vessels to general hypothermia, their reaction to local cooling was also examined. Local cooling was brought about by continual irrigation of the bulla with cold Ringer's solution in eight animals. Some data on the responses of the pial vessels during hypothermia were also obtained, again using the motion picture technique. These experiments were conducted on eight additional animals.

## RESULTS

*Respiration.* The self respired animal shows a gradual reduction in respiration rate and volume so that when the body temperature fell below 20° respiration was difficult to detect. In the artificially respired

animal, respiration was maintained at an arbitrary rate and stroke volume that previous observations indicated were compatible with maintaining normal conditions of cochlear blood flow and carotid blood pressure at normal temperature.

*Temperature.* A drop in rectal temperature of about .2° C per minute was obtained. This was more regular in the non-shivering, crurarized, respired animal than in the self respired animal with shivering. Shivering usually stopped in the latter group when temperature fell below 24° C.

*Heart.* An orderly drop in heart rate from 300 to 100 per minute with a good electrocardiogram was obtained down to about 20° C. As cooling continued below this temperature, marked slowing, cardiac irregularities, and complete cessation of activity were observed.

*Blood Pressure.* Blood pressure at the carotid increased approximately 35 per cent above normal (from about 60 to 80 mm Hg) soon after cooling commenced and remained elevated until the temperature decreased to around 22° C. Below 22° blood pressure dropped below normal and suddenly failed when the heart became irregular, weak and stopped (Fig. 1).

*Change of Vascular Elements.* The surgical preparation did not significantly alter the white blood count. Blood cells did not appear to adhere to one another or to the vessel wall as cooling continued even down to complete cessation of flow. There was no clear evidence of hemoconcentration or increased density of blood cells. As temperature dropped the number of white blood cells appearing in the field were reduced. This corresponded to a fall in the white blood count determined in the conventional manner and is consistent with the findings of others.[2]

*Rate of Blood Flow.* For both the self respired and artificially respired animals, it was not uncommon to see an increase in blood flow rate soon after the ice was placed on the animal. This appeared to be correlated with the sudden increase in blood pressure. After approximately ten to fifteen minutes, blood flow rate began to decrease. In the self respired animal an orderly fall in blood flow rate continued to about 24° when flow rate was reduced to as much as

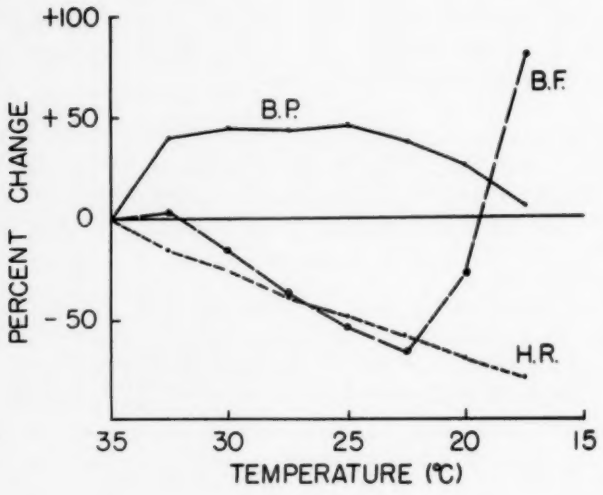


Fig. 1.—Graphs showing relation of cochlear blood flow rate (B.F.) during body cooling in self respired animal to blood pressure (B.P.) and heart rate (H.R.) Per cent of change is based on initial values at 35° C.

50% of normal. When cooling continued below this level an abrupt rise in flow rate occurred which might exceed the normal pre-cooled rate by 50 to 100% or more (Fig. 2). The observed change in flow rate occurred before blood pressure fell below the precooled level. If cooling continued further, cardiac and blood pressure failure soon followed along with cessation of blood flow. The reversal of flow rate mentioned above might be, in part, brought about by anoxia and an increase in $CO_2$ tension resulting from the suppressed respiration which took place at these low temperatures. Certainly $CO_2$ is effective in producing an increased blood flow rate at low temperature. For example, inhalation of 7% $CO_2$ in the artificially respired animal at 21.5° C produced a clear increase in flow rate through the cochlear vessels. In fact, the rate of increased flow at 21.5° was comparable to that found at near normal temperatures (Fig. 3). In the artificially respired animal, rate of flow dropped continuously throughout the cooling period (Fig. 4) without going through a phase of increased flow rate. Blood flow rate measured on animals which were not

subjected to hypothermia showed no consistent increase or decrease during the course of the experiments.

*Diameter of Vessels.* None of the vascular units in the fenestra showed definite changes in diameter even when cooling down to complete arrest of the heart and blood flow. For both self respired and artificially respired animals almost all vessels remained filled with cells even when flow stopped. Radiating arteriole, arteriovenous arcade, strial capillary and venules with diameters up to 15 μ were available for measurement (Fig. 5). Local cooling of these vessels by continuous irrigation even with Ringer's solution at 5° C did not produce a visible change in their calibre.

Pial vessels of 10 to 100 μ diameter under similar conditions of cooling did not reveal narrowing. In the self respired animal with deep hypothermia (20° C) dilation was clearly evident in vessels of about 100 μ diameter. These vessels became cyanotic and dilated about 30%.

## COMMENT

These findings on blood flow in the inner ear are in direct contrast to observations on the external ear during body cooling. Clark and Clark,[4] for example, found that in the rabbit ear chamber there were striking and rapid changes in diameter of small vessels even with a minimal drop in rectal temperature. The arteriovenous anastomoses contracted to lumen obliteration. Arteries were more responsive than veins. These vasoconstrictions greatly reduced the volume of blood circulated through the smaller vessels. Many received no blood while others received only serum or platelets. Flow rate was diminished and stasis or oscillation of flow was observed in many veins. The data from other experiments on blood flow in the rabbit ear, conducted under conditions of either general or local cooling, are in essential agreement, viz., local vasomotor activity markedly modifies flow rate.[5-7] Krogh[8] states that cold is a powerful stimulus for contraction of skin vessels. Contraction of arterioles, capillaries, and venules was produced in a 20° bath. If the bath was prolonged, capillaries and venules were found to relax while arteries remained contracted. Observation on the blood flow in the hamster pouch and the rat mesentery during hypothermia were recently reported by Lynch and Adolph.[9] They found that in the mesentery at low

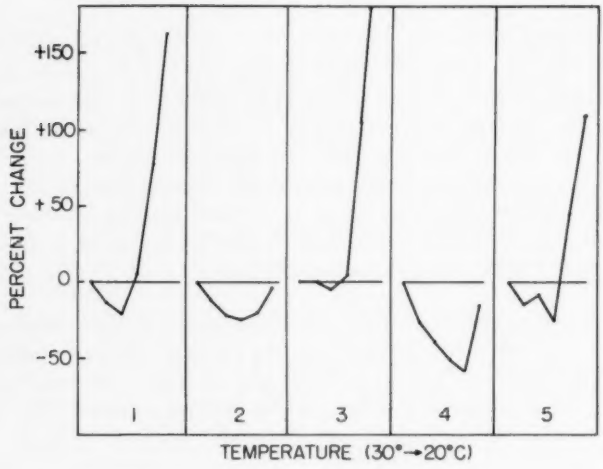


Fig. 2.—Graphs showing reversal of flow rate drop in 5 self respired animals cooled from 30 to 20° C. In 3 of these the flow rate at 20° exceeded that at 30° by 100% or more.

temperatures (20° C) flow stopped reversibly in about half of the capillaries and venules but on the average blood vessels did not narrow. Linear velocities decreased with temperature. As in the hamster cheek pouch the prevalence of local vasoconstriction was not related to temperature or cessation of flow. Furthermore, nearly all the vessels remained filled with blood. Stoppage of flow in capillaries increased as temperature decreased. These authors attributed the observed reduction in blood flow to a decrease in cardiac output and an increase in vascular resistance. Those factors which increased resistance to blood flow were hypothesized to be an increased viscosity of blood and a narrowing of the vessels outside the field of observation. Zweifach[10] reports that a drop in temperature of the fluid bathing the mesentery of over 2° C produced an extensive vasoconstriction and slowing of capillary flow.

From our study, it is clear that under conditions of reduced temperature the vessels of the inner ear do not respond like those of the

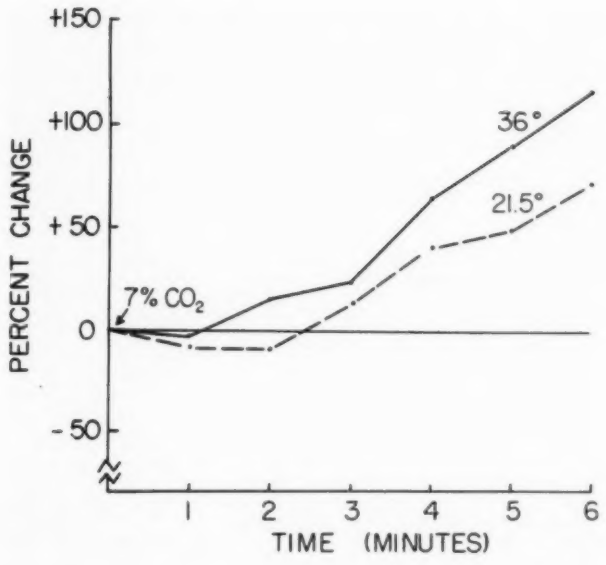


Fig. 3.—Graphs showing change in rate of cochlear blood flow with inhalation of 7% $CO_2$ at normal body temperature (36°) and in hypothermia (21.5°).

outer ear or skin. The behavior of the cochlear vessels during cooling is, instead, comparable to that of the cerebral vessels. Clark and Wentsler[11] found that the pial circulation observed in unanesthetized animals through cranial windows, was remarkably stable when body temperature was reduced. Meyer and Hunter[12] have used both photographic and polarographic methods to study cerebral blood flow during hypothermia. Whereas they reported vasoconstriction in larger vessels (200 μ) with decreased cerebral blood flow, they considered that these changes were brought about by a reduced cardiac output and fall in mean blood pressure, rather than by direct effects of low temperatures on the vessels themselves. In fact, placing ice directly on the pial vessels is ineffective for initiating diameter changes.[13] This corresponds to our findings and to the findings of Naumann et al[14] on local cooling of cochlear vessels.

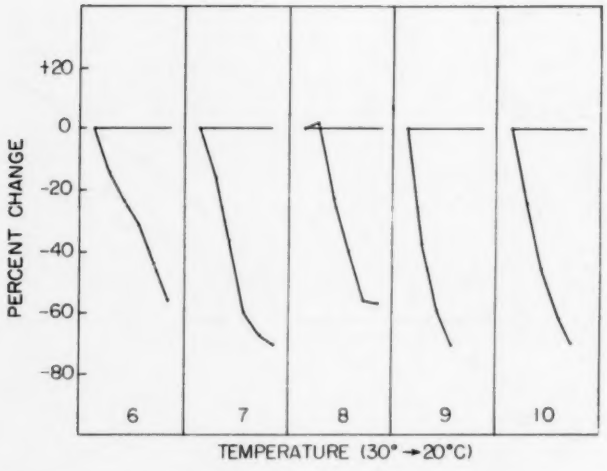


Fig. 4.—Graphs showing progressive drop in rate of cochlear blood flow during body cooling from 30° to 20° C in 5 curarized, artificially respired animals. Change in flow rate is recorded as per cent of rate at 30° C.

It appears that in hypothermia the circulation through the vital organs; i.e., brain and heart, is insured at the expense of the rest of the body by means of vasomotor occlusion of large areas of the peripheral vascular bed. The cochlear vessels are direct tributaries of the cerebral vessels. With cooling the heart rate drops while the stroke volume remains constant so that cardiac output per minute is reduced. This decrease in cardiac output, however, is proportional to the drop in oxygen consumption. Therefore the venous oxygen content and the arteriovenous difference in cerebral circulation remains rather constant during cooling.[15] Rosamoff and Holaday's[16] data on cerebral blood flow are consistent with this general statement, viz., reduced flow rate during hypothermia was proportional to reduced oxygen consumption.

The orderly fall in flow rate that we observed in the cochlear vessel in hypothermia was not due to local changes in the terminal vascular bed. Moreover slowing of blood flow cannot be attributed

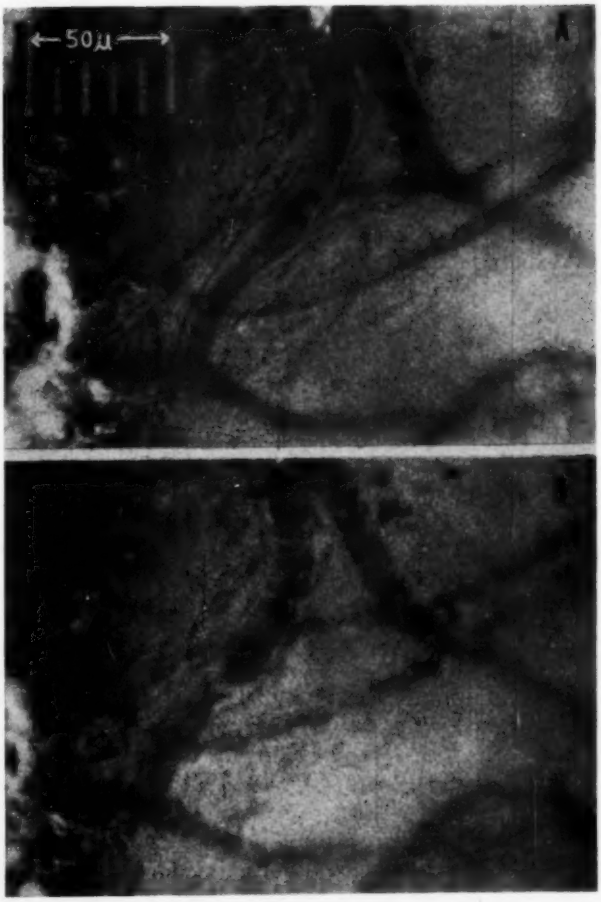


Fig. 5.—Cochlear fenestra showing radiating arteriole and strial vessels at normal temperature (A) and in deep hypothermia when flow has stopped (B). The diameter of the blood vessels remain essentially unchanged. Scale represents 50 micra. Each scene is a single frame from the moving picture record.

to agglutination of blood cells or to a fall in blood pressure. This is in contrast to the findings of Thuránszky[17] for a retinal blood flow in hypothermia. He reports a decreased flow rate that paralleled a decreased blood pressure in the cat. In our animals, except for the terminal stages, blood pressure increased rather than decreased during hypothermia. Since the perfusion pressure is maintained changes in resistance to flow is most likely responsible for gradual reduction in flow rate. The viscosity factor may be less important than Lynch and Adolph claim since we found an abrupt reversal of flow rate in deep hypothermia in the self respired animal. Furthermore the increase in cochlear blood flow rate with $CO_2$ administration in the hypothermic animal also suggests that the role of viscosity in impeding blood flow is of secondary importance to changes in the diameter of the vessels. The latter presumably occurred in the larger vessels outside of the field.

The relation of cardiac function to flow rate is clearly evident as the heart and blood pressure begin to fail. Blood flow slows, pulsates and finally stops. With rewarming and return of heart function and blood pressure flow is resumed. Throughout this period the observed vessels are not changed in diameter or the blood cells agglutinated. Under the limitation of our experimental conditions, spasm of cochlear vessels with interruption of blood flow does not appear to be a likely cause for dysfunction, since these events were never observed. In connection with cochlear function, it is worthwhile at this point to briefly consider its relation to blood flow during hypothermia.[17] Changes in neural activity of the cochlea are already evident at 34° when blood flow rate is not measurably reduced. At reduced temperatures, where cochlear blood flow is still 50% of normal, the function of the cochlea as reflected in the action potentials ($N_1$) is depressed to a greater extent or completely absent. At lower temperatures, comparable to those associated with increased flow rate, there is no improvement of these electrical responses. The decrease in the electrical output of the cochlea during hypothermia is therefore not directly related to the reduction of blood flow but probably to the reduced metabolism of the nerve cells. This separation between cochlear blood flow and cochlear function in hypothermia corresponds to the findings of Meyer and Hunter for the cortex.

Vascular responses to change in metabolism may be varied and the responses of the terminal, physiologically important, units are of

major importance. Changes in the total numbers of vessels carrying blood, changes in diameter of existing vessels, and changes in flow rate in these terminal vascular units are three vascular adjustments that may occur in response to changes in cell metabolism which serve to maintain homeostatic conditions for normal metabolism at the cell. Kety[18] shows that failure of these adjustments would rapidly cause a deficit in oxygen tension at the cell when its metabolism is increased above normal. In addition, the effect of oxygen tension gradients on the dissociation rates of oxyhemaglobin is important as well as changes in numbers and hemoglobin content of blood cells moving through the terminal vascular bed. In the cochlea, there appears to be but one major vascular adjustment to maintain homeostasis at the cell; that is change in flow rate through the terminal vascular units. Closing down of vessels, appearance of new vessels, shunting of flow through the arteriovenous arcades and dilation of existing vessels do not appear to be operating in this adjustment.

However by variation in extraction rate by the cell considerable variation in flow rate (½ to 2 x normal) is compatible with maintained normal function as in the brain. Similar relations for homeostasis of cell metabolism despite variations in rate of blood flow probably exist in the cochlea, and are probably associated with changes in the amount of oxygen extracted by the cochlear cells from the blood as it flows through the capillary. This would result in a constant adequate utilization of oxygen by the cell per unit of time despite variations in flow rate. However, when flow rate falls below some critical level, the cell can no longer obtain enough oxygen to maintain normal metabolism and function is seriously affected. An interesting example of the role of flow rate as a compensating mechanism in extreme biological emergencies has recently been furnished by Geiger.[19] By using up cell components the brain may function for an hour even in the absence of glucose if the cerebral blood flow rate is increased 300%.

## SUMMARY

Cochlear vessels are resistant to change in diameter even under the powerful vasomotor stimulation of profound rapid hypothermia.

Blood cells are not agglutinated or lysed even as blood flow comes to a complete stop.

Blood flow rate is reduced to about 50% normal but not stopped even when rectal temperature falls to 20° C, and below. Actually, there is a terminal rise in flow rate in deep hypothermia in self respired animals. This may be due to both anoxia and hypercapnia and is probably associated with dilation of cochlear and cerebral vessels outside of the observation window.

The moderate reduction in flow rate in hypothermia is probably due to increased resistance from viscosity changes and narrowing of vessels beyond the fenestra. Marked slowing of cochlear blood flow to complete stoppage follows closely the failing blood pressure as cooling continues to cardiac standstill.

The principal adjustment in the cochlear circulation to changing conditions, appears to be changes in the rate of blood flow through the vessels of the terminal vascular bed.

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LIX

# EXPERIMENTAL OBSERVATIONS ON POSTURAL NYSTAGMUS IN THE CAT

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This investigation deals with the physiological basis of the mechanism which produces postural nystagmus in laboratory animals. The vestibular disorder was induced by means of localized lesions in the sense organs or in the cerebellum. The results will be correlated with several postulates regarding the nature of postural nystagmus as seen in human cases. The hypothesis of Dix and Hallpike,[1] Lindsay and Hemenway[2] and Riesco[3] on the so-called "benign paroxysmal type" are to be considered in this report.

## THE HYPOTHESIS OF DIX AND HALLPIKE

The direction-fixed postural nystagmus of transitory type of Nylen[4] has been redefined by Dix and Hallpike[1] as a "benign paroxysmal type." The syndrome is characterized by the following features. The latency is of 5 to 6 seconds or less; the onset is heralded by distress and the appearance of nystagmus toward the affected ear when this is undermost; the course is a rapid crescendo, quick decline

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and disappearance. The return to the sitting position may produce a nystagmus in the opposite direction for a short time. Repetition of the postural test induces temporary extinction. Caloric and hearing tests may or may not be abnormal. Citron and Hallpike[5] postulated that this type of nystagmus is due to a qualitative disorder of the otolithic apparatus rather than a quantitative functional impairment. The stimulus leads to a vigorous, transient and abnormal discharge from the end organs which evokes the typical nystagmus reaction. The postulate that this disorder originates in the otolithic apparatus was based on the histologic findings in a human temporal bone. The microscopic examination showed absence of the otolithic membrane, disorganization of the sensory epithelium and certain gross tissue changes in the connective meshwork underlying the epithelium of the utricle of one ear. Similar changes but lesser in degree were present in the saccule. In the other ear, no abnormalities were found. The postulate that the mechanism which produces the nystagmus is a qualitative response of the affected otolithic apparatus was based upon the fact that the postural nystagmus was eliminated by surgical destruction of the affected labyrinth in two clinical cases.[5]

An attempt was made to reproduce the vestibular disorder reported by Dix and Hallpike[1] by producing a localized lesion in the otolithic apparatus of three cats.

The operation consisted of 1) exposing the attic by drilling down the superior wall of the external canal; 2) removal of incus, head of malleus and tensor tympani; during this step, damage to the tympanic membrane may occur; 3) fenestration of the otic capsule in the niche of the tensor tympani just behind the oval window and below the facial nerve; the fenestra was enlarged inward until the utricle and utricular nerve was identified; continuous irrigation with warm mammalian Ringer's solution prevents penetration of bone dust and blood into the vestibule; 4) section of the utricular nerve at the point where it emerges from the bony wall.

For exposing the lateral and superior ampullary nerves, the fenestra was enlarged upwards to just below the facial nerve. To prevent section or severe damage of the facial nerve, the fallopian canal was opened widely and the nerve retracted upward. This allows a sufficient field for exposing the ampulla of both lateral and superior semicircular canals and their corresponding nerves.

Section of utricular nerve produced a syndrome characterized by disequilibrium and spontaneous and postural nystagmus. Disturbances in equilibrium consisted of tilting of the nuchal region toward the operated ear, swaying of the body or the head or both and standing posture with limbs abducted. During motor performance, swaying increased and falling toward the operated side occurred frequently. The gait was broad based. This disequilibrium diminished with the passage of time. Full compensation was observed in about two weeks but tilting of the nuchal region toward the operated ear sometimes remained for a longer time.

Spontaneous horizontal nystagmus toward the unoperated ear was present for 24 hours only. It was of large amplitude and the frequency was 1 to 2 jerks per second. The postural test revealed that, with each change of position, the spontaneous nystagmus increased considerably in both amplitude and frequency, and occasionally presented a rotatory component toward the unoperated ear. After 24 hours, only postural nystagmus could be elicited. This could be direction-changing or direction-fixed; in either case, it was of a persistent type. Sooner or later (3 or 4 days) the nystagmus became a typical transitory direction-fixed type with the following features: the latency was short, 5 to 10 seconds or less; the course was of rapid crescendo followed by decline and disappearance in one to three mintues; the direction was consistently rotatory toward the unoperated ear but occasional jerks in other directions were sometimes observed; sometimes vocalization and struggling indicating distress were present; occasionally repeated postural tests produced extinction for several hours. After seven to ten days, postural nystagmus could no longer be elicited.

To determine whether operative trauma could be the cause of the vestibular disturbance already described, the vestibule of one cat was fenestrated as in the previous animals, and the utricular nerve exposed but not damaged. The postoperative follow-up showed no abnormalities in posture, motor performance or labyrinthine reflexes, and no spontaneous or postural nystagmus.

These experiments support the opinion of Dix and Hallpike that a lesion in the otolithic apparatus may be accompanied by postural nystagmus; but they do not answer the question whether the vestib-

ular disorder is due to damage in the utricular nerve or to activity of the other receptors as suggested by Lindsay and Hemenway.[2]

Although the temporal bones of these animals are not ready for microscopic studies, we assumed that the utricular nerve had been cut and therefore that the utricle was nonfunctioning. We also assume that the utricle and probably the sacculus of the human case reported by Dix and Hallpike were nonfunctioning or severely impaired as demonstrated by their illustrations and descriptions of the histopathology. These assumptions are hard to reconcile with the postulate that the vestibular disability was due to a qualitative disorder of the otolithic apparatus.

It must be clearly understood that similar lesions in the cat and in man do not produce similar syndromes in both species. The details will be described in other reports. We would like to mention only two differences; one, compensation of any vestibular disability in the cat takes place in a few days while in man the disability may persist for months or years. Two, duration of postural nystagmus of the so-called "benign paroxysmal type" is much longer in the cat (1 to 3 minutes) than in man (10 to 60 seconds).[4,6] These and other differences handicapped interpretation of the results to a certain extent, but the general trend of animal behavior provides useful information for the understanding of vestibular disability in human cases.

## THE HYPOTHESIS OF LINDSAY AND HEMENWAY

Lindsay and Hemenway[2] have questioned the otolithic origin of postural nystagmus for several reasons.

First, the possibility that a disturbance of the utricle alone is concerned with postural vertigo or postural nystagmus has not been clearly established. This argument is neither supported nor denied by the experiments on sectioning the utricular nerve.

Second, unilateral sudden total loss of vestibular function is not followed by postural nystagmus. This argument is sustained by clinical observations and it was confirmed experimentally in the cat. Unilateral labyrinthectomy was followed by the classical syndrome of disequilibrium and spontaneous nystagmus which increased in both amplitude and frequency with different head positions. Generally,

after the third postoperative day, the spontaneous nystagmus disappeared and none could be elicited with postural tests. Disturbances in equilibrium, however, may be observed for ten or more days. In one cat, bilateral labyrinthectomy was followed by a disturbance in posture and motor performance but no spontaneous or postural nystagmus was seen.

Third, stimulation of a utricle or saccule either directly in certain lower animals[7] or in man by physiological stimulation in the human centrifuge,[8] has failed to produce nystagmus. This argument was supported by the following experiments.

In three cats the nerves to utricle and horizontal and superior semicircular canals were exposed through a fenestra in the vestibule as described before. The first cat was immobilized by sectioning the brain stem above the superior colliculus. The nerves were stimulated with electric pulses delivered through a concentric electrode. Frequency, duration and voltage of the pulses were varied in several ways. Stimulation of the right lateral ampullary nerve produced a sustained deviation of the eyes toward the left and return to the midline when stimulus was discontinued. Stimulation of the right superior ampullary nerve produced a sustained deviation of the eyes toward the forehead. When the stimulus was discontinued, the eyes returned to midline position. Stimulation of the utricular nerve produced no eye movements at all. The deviation of the eyes following stimulation of both lateral and superior ampullary nerves seemed to represent the slow component of a provoked nystagmus. Absence of a fast component was attributed to shock following section of the brain stem. The second animal was immobilized by transection of the spinal cord at about the region of the decussation of the pyramids, and maintained alive by artificial respiration. Twenty minutes after the transection, the animal was conscious and presented spontaneous nystagmus toward the left. Fenestration of the right vestibule and exposure of the nerves preceded transection of the spinal cord. The spontaneous nystagmus following recovery of consciousness may be due to surgical trauma or to the fact that the circulation to the right lateral ampullary nerve was blocked. Stimulation of this nerve reversed the direction of the spontaneous nystagmus, that is, produced a nystagmus toward the stimulated ear. Stimulation of the superior ampullary nerve produced deviation of the eyes toward the forehead followed by vertical nystagmus toward the nose. When

the stimulation was discontinued, the spontaneous nystagmus resumed its previous beating. Stimulation of the utricular nerve produced no change in the rhythm of the spontaneous nystagmus but a slow deviation of the eyes occurred. Many trials clearly showed that the direction of slow movement of the eyes could not be predicted. These eye movements appeared to be related to the point on the nerve which was stimulated. The third animal was operated upon as was the previous one and the results of stimulation confirmed the observations already described. These findings are important because 1) they sustain the concept that stimulation of the utricular nerve[7,8] does not produce nystagmic reaction, and 2) they tend to confirm the hypothesis that postural nystagmus is not likely to be of otolithic origin. These experiments will be continued with more refined methods of stimulation.

Fourth, unilateral sudden partial loss of vestibular function seemed to be the situation which leads to postural nystagmus. Lindsay and Hemenway[2] supported this argument by the histologic findings in a human case with postural nystagmus. Microscopic examination of the right ear showed, 1) one or more large tortuous vessels displacing the nerve and many small vessels situated within Scarpa's ganglion in the internal auditory meatus; and 2) a marked degeneration of the ganglion cells in Scarpa's ganglion and degeneration of the nerve to the utricle and superior and horizontal semicircular canals. This human case was reproduced in one cat by sectioning the utricular nerve and the lateral and superior ampullary nerves of the right ear. The next day this cat presented pronounced disequilibrium and spontaneous nystagmus toward the left, of large amplitude and a frequency of 120 jerks per minute. Postural tests showed that both amplitude and frequency increased considerably without decay for two and one-half minutes of observation. On the second postoperative day, no spontaneous nystagmus was present but an irregular postural nystagmus appeared. It was mainly rotatory, clockwise, but suddenly changed to either vertical toward the nose or horizontal toward the left. On the third postoperative day, it was direction-fixed and of persistent type in the supine position, while, in both lateral left and hanging head positions, it was of transitory type (it lasted 90 seconds). After the sixth day, no more postural nystagmus could be elicited. The results of this experiment, which might be considered as a miniature of the human case reported by Lindsay and Hemenway, support their argument that postural nystagmus

follows unilateral sudden partial loss of vestibular function. The results also tend to support their postulate that, in these cases, the vestibular disorder is due to the presence of the remaining active receptors. The fact that, in both cat and human cases, the utricle is considered as nonfunctioning may however be used as an argument to sustain the hypothesis of otolithic origin of postural nystagmus. The postulate of Lindsay and Hemenway has a relevant consequence, i.e., the lesion may or may not involve the otolithic apparatus. In other words, if the loss of vestibular function is unilateral, sudden and partial, then the number and class of receptors which are damaged is not important. This and the previous argument prompted the following experiment.

The right lateral ampullary nerve was sectioned in one cat. Apparently, no other vestibular structures were damaged. The next day, there was pronounced disturbance of equilibrium and spontaneous nystagmus toward the left of large amplitude and 100 jerks per minute. The head was maintained erect and no tilting was observed on this or subsequent days. This finding indicates that the otolithic apparatus was not damaged. Postural tests showed an irregular nystagmus. In the supine position, it was first vertical toward the nose and then, at 90 seconds, changed to horizontal toward the left. In the other positions, the spontaneous nystagmus increased in both amplitude and frequency. On this second postoperative day, the spontaneous nystagmus was 42 jerks per minute. Postural tests revealed persistent rotatory nystagmus toward the left in the supine, lateral left and hanging head positions. In lateral right position, the frequency of the spontaneous nystagmus increased to 100 jerks per minute. On the third and subsequent days, no spontaneous nystagmus was observed, but a persistent direction-fixed type of postural nystagmus appeared after a latency of 5 to 20 seconds, depending on the position. The direction was rotatory toward the left. With the passage of time it diminished progressively, in both amplitude and frequency. It disappeared first in the lateral left and then in the lateral right position, while in the supine and hanging head positions, it was still elicited on the twelfth postoperative day. The importance of these experiments is that it supports the inference that impairment of otolithic apparatus is not necessary for producing postural nystagmus. This observation will be complemented by further experiments and the corresponding histopathological studies.

Recapitulating, the experiments on localized lesions in the vestibular receptors supported the hypothesis of Lindsay and Hemenway[2] which states that "The continuation of active impulses from part of the labyrinthine receptors with sudden loss (or impairment) of other receptors appears to be the situation which is characterized by postural vertigo and a positional nystagmus."

These observations on localized lesions of the vestibular sense organs will be complemented by further experiments. Also, the correlation of experimental findings and histopathology of the temporal bones remains to be done. So far, our results are to be considered as an interim report only.

## THE HYPOTHESIS OF RIESCO

The arguments of Riesco[3] regarding the origin of postural nystagmus follow.

Firstly, there is no evidence which demonstrates the existence of nystagmus of otolithic origin. This argument is supported by our experiments on stimulation of utricular nerve.

Secondly, in his experience in the absence of auditory disturbances only a few cases of postural vertigo with postural nystagmus can be correlated with peripheral lesions. Although this argument was not considered in our experiments, it is supported by clinical cases of postural vertigo and postural nystagmus with normal responses to vestibular tests.

Thirdly, postural nystagmus may be due in many cases to a state of hyperexcitability of the vestibular nuclei. In cases of a benign paroxysmal type, he postulated that the incoming, normal signals, which arise in the vestibular receptors through change in position of the head, produced a qualitatively abnormal response of the nerve cells in the vestibular nuclei. The abnormal response determines the transient and paroxysmal characteristics of the postural nystagmus. Riesco[3] supports this hypothesis with the surgical findings in a human case with astrocytoma of the inferior vermis of the cerebellum. This patient had a benign paroxysmal type postural nystagmus and postural vertigo with no signs of peripheral lesions.

A series of 51 experiments on ablation of individual segments of cerebellum, supported the postulate of Riesco that the so-called "benign paroxysmal type" of postural nystagmus may be produced by lesions in the central nervous system. These experiments showed that only a lesion limited to either nodulus or flocculus produced a syndrome characterized by disequilibrium and a direction-fixed postural nystagmus of transitory type. However, the present report is concerned only with results of lesions in the nodulus.

Craniotomy is done by removing the squamous part of the occipital bone between the superior nuchal line and the foramen magnum. After incision of the meninges, the uvula is carefully elevated until the fourth ventricle and the nodulus are exposed. During this step the tela chorioidea and the chorioid plexus are partially removed. Finally, the nodulus is ablated by suction with fine pipettes. The hemorrhage is minimal and easily controlled.

The disturbance of equilibrium was characterized by swaying of the trunk or the head, or both, abduction of the limbs, a broad base gait, and falling toward the right or left during motor performance. This disorder appeared in all animals with normal labyrinths as well as in those with bilateral labyrinthectomy. Apparently, equilibratory compensation took place within 30 days. These findings indicate that, functionally, the nodulus is concerned with maintenance of equilibrium. The question as to whether its influence is mediated through the vestibular system or some other mechanism remains to be answered. It is interesting to note that no signs of cerebellar ataxia were present.

Spontaneous nystagmus was not seen in this series, while postural nystagmus was a consistent finding. Its latency, onset, course and duration closely coincided with the description given by Dix and Hallpike[1] and Citron and Hallpike[5] of the "benign paroxysmal type" of postural nystagmus seen in human cases. It is known that, in many instances, the disorder which produces this type of nystagmus tends to recover with time and simple sedative measures. As pointed out by Riesco, this fact does not justify the use of the term "benign" since it implies that the disorder is associated with peripheral lesions or with pathology of a simple nature. On the other hand, the term "paroxysmal" identifies the signs of a clear cut syndrome but does not identify its etiology. For this and practical reasons, we continue

to use the term "paroxysmal type" to designate the "transitory direction-fixed type" of postural nystagmus of Nylén.[4] As suggested by Aschan et al,[10] the incorporation of the terms "persistent" and "transitory" in the classification of Nylén could be advantageous.

Previous investigations[10-17] strongly support the theory that the paleocerebellum, mainly the flocculonodular lobe, acts as an inhibitor of the labyrinthine reflexes. It is assumed that the inhibitory action is upon the vestibular centers but its neural mechanism is unknown. The results of our experiments support this theory, and furthermore, emphasize the point that the release of vestibular centers from cerebellar inhibition seemed to be sufficient for evoking postural nystagmus. Riesco was essentially right when he stated that postural nystagmus of paroxysmal type may be explained as a qualitatively abnormal response of the vestibular nuclei to the postural stimulus. He did not realize however, that the qualitatively abnormal response may be due to a release of vestibular centers from cerebellar inhibition. Spiegel and Scala[9] proposed the hypothesis that lack of cerebellar inhibition produces a state of hyperexcitability of the vestibular nuclei. This idea may be correct but further investigation is required.

The possibility, that the postural nystagmus, following removal of the nodulus, is due to irritation of the vestibular nuclei by surgical trauma, was ruled out by the results of the control experiments. In these animals, the fourth ventricle was opened and exposed as far as the lingula. The tela chorioidea and the chorioid plexus were partially removed and hemorrhage was intentionally produced. Damage to the nodulus or other cerebellar and medullary structures were avoided. In some animals, foreign bodies such as clots of blood, pieces of gelfoam and bone wax were left in the cavity of the fourth ventricle. These control animals showed no disturbances of equilibrium or spontaneous or postural nystagmus at any time.

Ablation of the nodulus in the cat reproduces approximately the symptoms of the human case reported by Riesco. As in the case of peripheral lesions, a striking difference exists between the two species. The cat compensates for the disability in one to three weeks while in the human case,[3] postural nystagmus was observed for one year before the operation and for another year after removal of the astrocytoma.

The hypothesis of Riesco on the neural mechanism of postural nystagmus of central origin, emphasized the role of signals from peripheral receptors indicating positional change of the head. Those signals cause an abnormal response of the vestibular nuclei, when these are in a state of hyperexcitability, or as we postulate, when they are released from cerebellar inhibition. The following experiments demonstrate that the presence of these signals is necessary to produce postural nystagmus of cerebellar origin.

Postural nystagmus which followed removal of the nodulus was temporarily eliminated (about five hours) by cocainization of both ears, and it disappeared permanently following bilateral labyrinthectomy. Bilateral labyrinthectomy followed by removal of the nodulus failed to produce postural nystagmus. These findings clearly demonstrate that signals from vestibular receptors, indicating the positional change of the head, are necessary for producing postural nystagmus. The elimination of postural nystagmus of cerebellar origin by bilateral labyrinthectomy or cocainization has, as Allen and Fernández[18] pointed out, an important bearing from the clinical point of view. That is, when destruction of the vestibular organ by operation or disease abolishes positional nystagmus, it does not necessarily follow that the positional nystagmus was caused by a lesion in that organ.

Recapituating, these ablation experiments are significant for two reasons. Firstly, the disturbance in equilibrium, which appeared in normal as well as bilateral labyrinthectomized animals, indicates that the flocculonodular lobe plays an important role in maintenance of equilibrium independently of the vestibular receptors. Secondly, the appearance of postural nystagmus and its elimination by bilateral labyrinthectomy supports the concept of functional relations between flocculonodular lobe and vestibular system.

## SUMMARY

The investigation deals with the physiological basis that underlies the release of postural nystagmus as seen in laboratory animals. The effect of localized lesions in the vestibular receptors or in the cerebellum was studied in a series of cats. The observations on localized lesions in the end organ represented an interim report which will be complemented by further experiments, while the observations on localized lesions in the cerebellum may be considered as final.

Section of one utricular nerve produced spontaneous nystagmus toward the unoperated ear for 24 hours, followed first by a direction-changing postural nystagmus and later by a benign paroxysmal type. No spontaneous or postural nystagmus was observed after the seventh day. These observations support the theory that a lesion in the otolithic apparatus may be accompanied by postural nystagmus. The experiments did not clarify, however, the question as to whether the vestibular disorder was due to damage in the nervus utricularis or to activity of the other receptors.

Unilateral labyrinthectomy produced spontaneous nystagmus which lasted for about three days. It was not accompanied or followed by postural nystagmus. This observation supports the opinion that sudden unilateral loss of vestibular function is not followed by postural nystagmus.

Unilateral section of the nervus utricularis and the nervus ampullares lateralis et superior produced a spontaneous nystagmus toward the unoperated ear followed by postural nystagmus which lasted about six days. This observation supports the theory that unilateral sudden partial loss of vestibular function may be followed by postural nystagmus.

Electrical stimulation of the nervus ampullaris lateralis in the conscious cat, provoked horizontal nystagmus toward the stimulated ear while stimulation of the nervus ampullaris superior provoked vertical nystagmus toward the nose.

Stimulation of the nervus utricularis did not produce nystagmus but it provoked deviation of the eyes in several directions; the direction of these eye movements appears to be related to the point on the nerve which is stimulated. This observation supports the theory that postural nystagmus is not likely to be of otolithic origin.

Section of the nervus ampullaris lateralis alone produced a syndrome very similar to section of the nervus utricularis alone. The main difference between the two syndromes was that, in section of the nervus ampullaris lateralis, no tilting of the head toward the operated side was observed. Lesions localized to or including the nervus utricularis consistently produced tilting of the head toward the operated ear. These observations tend to confirm the hypothesis

that the postural nystagmus following unilateral sudden partial loss of vestibular function may be due to the activity of remaining vestibular receptors. These findings also indicate that a lesion in the otolithic apparatus is not a necessary accompaniment for releasing postural nystagmus. The histologic preparation of these temporal bones with localized lesions is not yet completed for microscopic studies.

Lesions of the cerebellum localized to, or including parts of, the flocculonodular lobe consistently produced a syndrome characterized by disequilibrium and postural nystagmus of benign paroxysmal type. This tends to confirm the suggestion that postural nystagmus of benign paroxysmal type may be produced by a lesion in the central nervous system. The use of the term "benign" is misleading because it implies that this type of postural nystagmus is associated with peripheral lesions or with pathology of simple nature. The release of vestibular centers from cerebellar inhibition appears from this finding, to be sufficient for producing postural nystagmus of this type.

Postural nystagmus produced by ablation of the nodulus was temporarily eliminated by cocainization of both labyrinths, while surgical bilateral labyrinthectomy produced a permanent disappearance. Surgical bilateral labyrinthectomy followed by ablation of nodulus failed to produce postural nystagmus. This would indicate that the presence of signals with information as to the position of head in space is necessary for producing the postural nystagmus of cerebellar origin. It is pointed out that disappearance of postural nystagmus by disease or unilateral labyrinthectomy does not necessarily mean that positional nystagmus originated in the vestibular sense organ.

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LX

# SUDDEN DEAFNESS AND BELL'S PALSY: A COMMON CAUSE

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The purpose of this paper is twofold: to report, first, an investigation of the cause of sudden, severe nerve deafness and, second, a parallel investigation of the cause of Bell's palsy.

In 1957, van Dishoeck[1] reported 100 cases of sudden deafness. Of these, 14 were caused by mumps and 14 by other viral diseases. The diagnosis was established by using viral antigens and complement fixation methods. Although other writers have speculated that viral diseases may sometimes cause sudden deafness, apparently none, except van Dishoeck, have used complement fixation methods to establish the relationship between sudden deafness and viral disease.

It is well known that epidemic parotitis (clinical mumps) may be complicated by nerve deafness. What is not generally recognized is that some patients have mumps without parotitis, just as others have poliomyelitis without paralysis. A few patients who have mumps without parotitis develop deafness. It is this group that concerns us now.

## THE CONTROL GROUP

Three hundred and seventy patients, all unselected adult routine admissions to the University Hospital Out-patient Clinic, were used

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as a control group. Blood specimens from these patients were sent to the Ohio State Virology Laboratory. Except for a code number, the specimens were unmarked. There was no means by which the one laboratory technican (who ran all our tests) could distinguish the control specimens from identical specimens drawn from patients with sudden deafness.

*The Complement Fixation Tests.* Serologic methods were used to test for antibodies produced by mumps and by influenza, types A and B. There were no positive titers for influenza. Antibodies for mumps were found in some patients with sudden deafness and also in some patients in the control group.

Mumps antibody titers are among the most reliable and consistent of all virus antibody tests. In order to evaluate the significance of the laboratory tests, we must explain briefly about previously established standards as well as about our own results.

*Mumps Viral Antigen.* According to laboratory authorities,[2] a diagnosis of mumps is considered when a blood specimen, after being diluted at least 64 times, reacts with the mumps viral antigen. (In other words, a titer of 64 or above is positive but the next dilution under 64, which is 32, is not positive.)

On this basis, in our control series of 370 patients, only nine patients, or 2.5 per cent, had positive titers. The incidence of 2.5 per cent in our control series is important to keep in mind because it is against this figure, derived from 370 unselected patients, that our clinical data must be evaluated.

*Soluble Antigen.* Besides the regular viral antigen, a so-called soluble antigen may be used in mumps complement fixation tests. Soluble antigen measures antibodies that appear within a week or two after symptoms develop. Generally, these titers drop sooner than those measuerd by the mumps viral antigen, which may remain elevated for six months or a year.

When soluble antigen was used, only two of the nine patients in our control group who had shown titers of 64 with mumps viral antigen, now had elevated titers—and both of these patients had mumps with parotitis. In other words, except for the two patients

with mumps parotitis, there was no patient in our control series who had an elevated titer for both the mumps viral antigen and the soluble antigen.

### PATIENTS WITH SUDDEN DEAFNESS

In the last year, we examined *nine* patients with sudden, severe unilateral nerve deafness. Of these, four had mumps and two others probably had mumps. None of the patients had parotitis.

Before giving the laboratory findings, we will discuss briefly symptoms and audiometric findings. To do so is important, because, as we found, after examining other patients sent to us for sudden, severe, nerve deafness, these terms do not mean the same to everyone.

Although not pathognomonic, the deafness associated with mumps is clear-cut. The diagnosis may be suspected as soon as the history is taken and a few simple audiometric tests done. Here are the characteristic features: *First*, the onset of deafness is very abrupt, sometimes instantaneous. One patient, for example, heard a click in her ear and knew she was deaf. Others, who went to bed with normal hearing, woke up deaf. *Second*, the deafness associated with mumps is very severe. Initially, most patients could not understand a loud shout near the affected ear. *Third*, in each of our patients with mumps, the deafness was unilateral (although van Dishoeck reported bilateral cases). *Fourth*, the hearing usually improves.

*Discrimination* scores were initially very poor in all patients. Later, the scores of three patients approached normal. The other scores remained below 30 per cent.

Recruitment (incomplete) was present in three patients. Of the three showing no recruitment, one was totally deaf and one had regained normal hearing by the time recruitment tests were done.

*Hearing Improvement.* One patient regained almost normal hearing within three weeks. Four improved from no hearing, or hearing at the 90 decibel level, to hearing at the 40 to 60 decibel level.

Only one patient has failed to regain hearing. She has remained almost totally deaf.

AUDIOMETRIC FINDINGS

L.T., 35 years, female. Sudden deafness 2-26-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 3-3-58 | — | — | — | — | — | — |
| 3-3-59 | 70 | 55 | 55 | 40 | 80 | — |

Severe vertigo and tinnitus.
Final discrimination 16%.
Viral antigen titer 128 (positive).

H.W., 49 years, male. Sudden deafness 9-26-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 9-30-58 | 35 | 55 | 60 | 35 | 40 | 45 |
| 10-14-58 | 10 | 0 | 10 | 10 | 10 | 5 |

No vertigo. Mild tinnitus.
Viral antigen titer 64 (positive).
Hearing already "much better" when we first tested him.

E.B., 30 years, male. Sudden deafness 8-13-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 8-18-58 | | | | 95 | 95 | 80 |
| 2-10-59 | 40m | 40 | 35 | 30 | 50 | |

Severe vertigo. Moderate tinnitus.
Final discrimination 92%.
Viral antigen titer 64 (positive).

A.B., 9 years, female. Sudden deafness 8-15-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 10-22-58 | 70 | 90 | 95 | 90 | 95 | |
| 2-3-59 | 60 | 65 | 65 | 65 | 65 | 80 |

Moderate vertigo and tinnitus.
Final discrimination 44%.
Viral antigen titer 64 (positive).

L.S., 51 years, female. Sudden deafness 9-29-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 12-29-58 | | | | | | |
| 2-10-59 | 80 | 85 | | | | |

Moderate vertigo. No tinnitus.
Final discrimination 0.
Viral antigen titer 32 (probably positive when soluble antigen titer considered).

C.M., 44 years, male. Sudden deafness 10-25-58

| | 256 | 512 | 1024 | 2048 | 4096 | 8192 |
|---|---|---|---|---|---|---|
| 11-12-58 | 80 | 80 | 100 | 95 | 100 | 80 |
| 2-10-59 | | 40 | 40 | 45 | | |

Moderate vertigo and tinnitus.
Final discrimination 86%.
Viral antigen titer 32 (probably positive when soluble antigen titer considered).

Tests for functional deafness were done on each patient. These included the delayed sidetone test, electrodermal audiometry and the Doerfler-Stewart test. All patients were cleared with respect to malingering and functional deafness.

*Tinnitus* was present in five patients. Only one patient found the tinnitus excessively loud.

*Vertigo* was present in three patients. One patient was very sick and vomited for a week. The other two were only mildly incapacitated.

*The Caloric Reactions.* Caloric tests were done on all patients. Water at 110, 86 and 68 degrees Fahrenheit was used.

Except for one patient who was sick for a week, there was no good correlation between the severity of vertigo and the caloric reaction. This patient, who had a dead labyrinth when first tested (no response to ice water), eventually responded to 68 degree water. Three patients had normal caloric reactions. Two had unilateral hypoactivity.

*Previous Mumps.* Each patient clearly recalled a previous childhood mumps infection.

*Upper Respiratory Infection.* A recent upper respiratory infection, which preceded the deafness by about ten days, was remembered by four patients and denied by two.

*Physical Examination.* The physical examination was normal in all patients. Particularly, the tympanic membranes were normal.

*The Patients Without Mumps.* In our series of nine patients with sudden deafness, there were three who did not have a positive titer for mumps. Nevertheless, the symptoms and findings in these patients were almost identical to those who did have mumps. Two became deaf instantaneously and the third lost his hearing over a period of several hours. In all three, the severity of deafness was measured as greater than a 90 decibel loss. Discrimination scores were extremely low. All had moderate to severe vertigo.

## COMMENT

Besides mumps, there are, of course, other conditions that cause sudden deafness. At least two other viral diseases, influenza and poliomyelitis, have been implicated by van Dishoeck. There are still other viral diseases, for example, measles, for which reliable antibody tests are not available. We believe it very likely that other viral diseases may have caused the deafness of our three patients who did not have mumps.

In addition to viral infections, other conditions also cause sudden deafness. High on the list have been vascular accidents affecting the internal auditory artery. But patients do not die of their supposed thromboses and the diagnosis of vascular accident is hard to prove. We believe this explanation of sudden deafness has been overemphasized.

The exact mechanism by which mumps produces deafness is not known. We could find no published reports concerning post mortem examinations of patients with deafness due to mumps.

## CONCLUSIONS

1. Mumps (without parotitis) is a common cause of sudden, severe nerve deafness. In our patients, mumps deafness has been unilateral only.

2. The affected ear may recover completely, there may be partial recovery, or the deafness may remain total.

3. Recruitment is usually present.

4. Vertigo is not always associated with mumps deafness. Results of caloric tests do not correlate well with the presence or absence of vertigo.

5. All patients had previously had mumps.

## BELL'S PALSY

The second group of patients that we examined had Bell's palsy. By Bell's palsy, we mean a facial paralysis that is unexplained by

anything in the physical or laboratory examinations. Usually the condition is called idiopathic and is attributed to a vascular spasm and ischemia of the descending portion of the facial nerve. Most patients recover spontaneously. The condition is too well known to require further description.

We examined ten patients with undisputed Bell's palsy. Of these, four had elevated titers for mumps. Their titers were 256, 256, 128, and 64. The titer needed for the diagnosis of mumps is 64. In our control series of 370 patients, only 9 titers of 64 were found. When soluble antigen was used for additional testing, only two positive titers remained. Both of these patients had clinical mumps. On the other hand, all four patients with Bell's palsy due to mumps showed elevated titers with soluble antigen.

We conclude that mumps is a common cause of Bell's palsy.

## COMMENT

There may be an analogy between the manner in which mumps produces facial paralysis and the manner in which the herpes simplex virus causes recurrent stomatitis. In case of infections with the herpes simplex virus, some authorities believe that we contract the initial infection in childhood, when, in addition to the mucous membrane lesions, there is often a severe constitutional reaction. Thereafter, the herpes simplex virus resides locally in the tissue. Later in life, recurrent herpetic lesions in the mouth or on the lips develop after minor trauma. But, because of circulating antibodies, there is no constitutional reaction.

Although we have no experimental evidence indicating that a similar mechanism may explain how mumps can produce facial paralysis, certain similarities are apparent. In Bell's palsy, the old explanation of a cold wind striking the face may take on new significance. The cold wind, or similar trauma coming at just the right time, may be the stimulus needed to reactivate a mumps infection that for years had been dormant in the parotid gland. On the other hand, Bell's palsy sometimes occurs simultaneously in more than one member of a family. In these instances, an exogenous infection may be suspected.

Of course, many presently unanswerable questions come to mind. Is there swelling of the terminal branches of the facial nerve as well

as swelling of the nerve trunk? Why is facial paralysis never a part of mumps parotitis? In the case of mumps deafness, are we dealing with a reactivation of an old infection?

Clinical and laboratory experiments now under way may help answer these and other problems.

SUMMARY

Mumps and influenza antibody titer determinations were done on blood specimens from 370 unselected patients (the control group). The same tests were made on blood specimens from nine patients with sudden, severe nerve deafness and ten patients with Bell's palsy. The results indicate that subclinical mumps is a common cause of both sudden deafness and Bell's palsy.

OHIO STATE UNIVERSITY

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We are greatly indebted to Dr. George Anderson, Chief of the Virus Station, Ohio Department of Health Laboratories, and his assistant, Mr. Don Keiper, for performing over 1000 complement fixation tests and giving authoritative opinions concerning their interpretation. We also express our gratitude to Dr. John O'Neill, Associate Professor, Department of Speech, Ohio State University, who performed the advanced audiometric studies necessary to exclude patients with functional deafness.

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LXI

# CERTAIN PROBLEMS IN TYMPANOPLASTY

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Since the first report of tympanoplasty techniques by Moritz, Thullen, Wullstein and Zollner in 1950[1] there have been numerous papers[2-7] concerning the theory, classification, progress and results of tympanoplasty. Wullstein[8] has presented a clear and concise classification and application of the various types of tympanoplasty. Rather than reiterate such details which have been adequately covered in the literature, a discussion concerning certain problems of tympanoplasty appears to be appropriate. In any discussion on tympanoplasty it is well to repeat the objectives or supreme rule (Oberstes Gebot) of Wullstein: first, control the pathology in the temporal bone and eliminate possible complications, and secondly, attempt to improve the hearing by reconstruction techniques. The systematic application of the detailed techniques described by Wullstein[8] and Zollner[10] result in a high percentage of otologically rehabilitated patients measuring up to this prime objective. However, certain problems are apparent in the application of the technique.

## PREPARATION OF THE SURGEON

Tympanoplasty taxes the total skills and ingenuity of the otologic surgeon more than any other procedure, since it may require, in any given case, most of the operative techniques which apply to the temporal bone. Meticulous techniques in mastoid surgery plus the rehabilitative procedures of stapes mobilization, reconstruction of the middle ear conduction mechanism, including the tympanic membrane, and fenestration surgery are required for adequate results. It is possible that enthusiasm for the procedure has exceeded the general development of the required skills in our specialty. We believe that a more thorough and basic training in our residency program in diseases and surgery of the temporal bone is indicated before the procedure can be included in the general surgical armentarium of the otolaryngologist. The short course does not appear to be the medium

for the preparation of the tympanoplastic surgeon. Adequate experience is necessary for the recognition of the complicated case preoperatively. Mature surgical judgment is demanded for the proper application of operative techniques.

## CONTROL OF SUPPURATION AND TEMPORAL BONE PATHOLOGY

Infections limited to the middle ear in the absence of cholesteatoma may often be controlled by conservative measures. The routine use of culture and sensitivity tests and specific local and systemic antibiotics, when available, is required. Burow's solution, gentian violet or 25% argyrol solution may be applied locally when the tests reveal the organism insensitive to specific antibiotics. In order to obtain more adequate contact of the drug on the mucosa in the various recesses in the middle ear we aspirate the middle ear at intervals of 48 hours and administer the drug in solution through a cannula directly into the involved area.

When the infection is apparently controlled in this manner and the ear has been dry for a period of four to six weeks without treatment, a type I or type II tympanoplasty may be performed (Table I).

TABLE I

CONSERVATIVE MEASURES

| | | |
|---|---|---|
| Cases with No Primary Infection | 91 | |
| Postoperative Perforations | 16 | (17.6%) |
| Cases with Primary Infection | 120 | |
| Postoperative Perforations | 38 | (31.6%) |

In cases of persistent mastoid infection, again in the absence of cholesteatoma, the procedure may be done in two stages. The first stage consists of a thorough simple or modified radical mastoidectomy and adequate follow-up therapy as applied to suppuration limited to the middle ear. If simple mastoidectomy is performed a polyethylene tube may be placed through a stab incision in the upper portion of the postauricular sulcus to be used as a cannula for instillation of a specific antibiotic solution into the mastoid cavity twice weekly for a two week period. Local therapy to the middle ear and systemic

therapy are administered as indicated. After all traces of suppuration are absent from the middle ear for an eight week period without treatment a type I or type II tympanoplasty may be performed. In this manner the external auditory canal is maintained and an open mastoid cavity is avoided (Table II).

TABLE II

SIMPLE MASTOIDECTOMY

| | | |
|---|---|---|
| 1. | At time of myringoplasty<br>One developed infection<br>one month postoperatively | 11 |
| 2. | Before myringoplasty<br>None developed infection<br>postoperatively | 4 |

When modified radical mastoidectomy is necessary a thin area of the bridge may be left in place, when possible, to protect the intact ossicular chain. Specific antibiotics in irrigating solutions during surgery and to saturate the packs in the cavity are recommended.

The presence of cholesteatoma indicates radical mastoidectomy and tympanoplastic repair in one or two stages, except in cases in which a small cholesteatoma localized in the epitympanum lies lateral to or above the ossicles. When hearing losses are associated with the latter type of cholesteatoma, we use a modified Tumarkin[11] approach to remove a portion of the tympanic plate overlying the involved area. The small cholesteatoma sac is enucleated and the appropriate tympanoplastic procedure is used to close the resulting defect in the epitympanum and middle ear. The presence of cholesteatoma matrix medial to the incus and head of the malleus in the mastoid antrum requires the radical approach and removal of all vestiges of matrix before application of the tympanoplastic graft. When the sinus tympani is large and involved with cholesteatoma matrix, we consider the sinus tympani to be inaccessible as far as complete removal of matrix is concerned.

In the usual case with cholesteatoma and minimal associated suppuration in the mastoid and middle ear, the procedure is done in one stage. However in the presence of active suppuration and granula-

tions in the middle ear, a two stage procedure is employed. Removal of the cholesteatoma matrix and granulation tissue from the middle ear and mastoid are done as the first stage. Systemic and local specific therapy follows, with secondary skin grafting of the resultant mastoid bowl two weeks postoperatively. After the middle ear has been dry for an eight week period in the absence of therapy, the appropriate tympanic graft may be applied as the second stage (Table III).

TABLE III

MODIFIED RADICAL OR RADICAL MASTOIDECTOMY

| | |
|---|---|
| Total Cases | 29 |
| Postoperative Perforation of Graft | 7 (24.1%) |

## CLINICAL EVALUATION OF THE HEARING IMPAIRMENT

In addition to routine air and bone conduction, speech reception threshold and discrimination tests, special studies of the sound conduction mechanism are indicated. Patients having small and moderate sized central perforations are given a "patch test" when feasible. After the preliminary tests are completed, a paper patch is applied to the tympanic membrane perforation and an air conduction test is made with the patch in place. If the patch can be applied successfully, completely sealing the middle ear around the periphery of the perforation, valuable information concerning the integrity and function of the ossicular chain may be obtained. In those cases where it is not feasible to successfully apply a patch because of the size or location of the perforation, an acoustic probe is used to study the ossicular chain. In the presence of cholesteatoma, the acoustic probe test may not be reliable, since it is possible for the cholesteatomatous mass to act as a conducting mechanism between the parts of a disrupted ossicular chain. In those cases with cholesteatoma the ossicular chain is inspected for continuity and tested for mobility during surgery. Clinical experience is essential for proper evaluation of the functional status of the ossicular chain and window areas.

An accurate study of the hearing impairment allows for possible planned restoration of hearing depending on the extent of the pathology and the degree of the conduction loss.

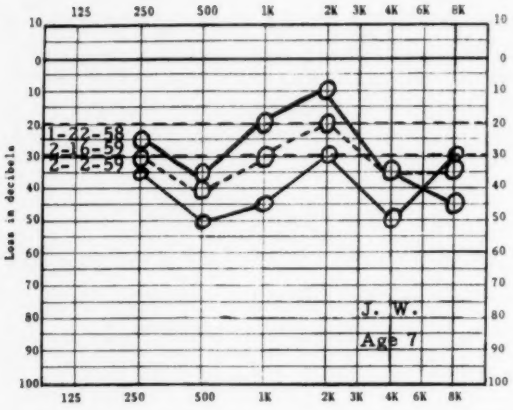


Fig. 1.—Fluctuation of hearing as a result of eustachian tube dysfunction incident to recurrent sinusitis and secondary otitis media with effusion. 1-22-58: postoperative level of type III tympanoplasty; 2-2-59: level with effusion secondary to sinusitis; 2-16-59: hearing level after control of sinus infection and partial clearing of middle ear.

## PROBLEMS OF EUSTACHIAN TUBE FUNCTION

Dysfunction of the eustachian tube is an important current problem in tympanoplasty. Chronic perforations are often a result of eustachian tube insufficiency. Closure of the middle ear space by application of a tympanic graft in such an ear often leads to the complication of chronic middle ear effusion, development of a retraction pocket in the graft or recurrent middle ear infection and slough of the graft.

Preoperative tests such as politzerization, the Valsalva procedure and catheterization and inflation of the tube may be helpful but are inadequate as an indication of true function. Zöllner[12] studied eustachian tube function by measuring the pressure in the nasopharynx required to move the tympanic membrane during swallowing. Compere[13] studies eustachian tube function by the use of contrast media in the middle ear followed by a measure with roentgenograms of the evacuation time of the material through the eustachian tube.

TABLE IV

*Example of Check List Used for Each Patient Prior to Surgery*

CHECK LIST FOR PREOPERATIVE STUDIES ON TYMPANOPLASTY AND MYRINGOPLASTY PATIENTS

1. Culture and sensitivity
2. Mastoid x-rays
3. Hearing tests
   - A. Air-bone gap
   - B. Patch tests (air conduction)
     1. Before patch
     2. After patch
   - C. Acoustic probe
     1. Promontory
     2. Malleus
4. Eustachian tube function
   - A. Calibrated politzeration
   - B. Examination of upper respiratory tract
     1. Nasopharynx
     2. Nose
     3. Sinus
     4. Allergy
5. Condition of middle ear
   - A. Air space
   - B. Middle ear mucosa

These preoperative tests undoubtedly supply valuable information, but in their interpretation one should consider that they may be of only transient value. The tests may have been done under ideal conditions. The true test of eustachian tube insufficiency occurs once the middle ear is sealed by the graft. Under ideal conditions the tube may be barely adequate in function but in times of stress such as during a recurrent sinus infection, the function may be totally inadequate. For this reason a careful preoperative examination should be made to rule out or control allergic rhinitis, recurrent sinus suppuration, and chronic hypertrophy and infection of the adenoid area. Any of these conditions may precipitate eustachian tube insufficiency and postoperative complications. A sound review of the history and careful physical examination of the upper respiratory tract preoperatively is mandatory. When faced with an obviously non-functioning eustachian tube we have not attempted reconstruction methods on the tube.

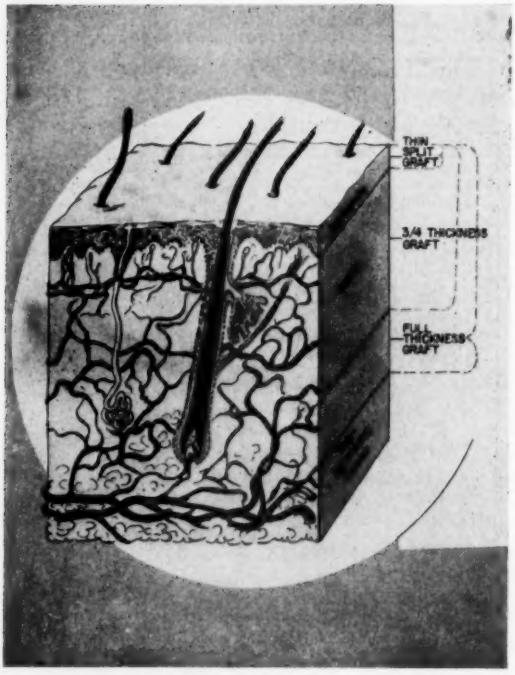


Figure 2

Many surgeons are now attacking the problem of reconstruction of the eustachian tube. In view of the varied complicating factors present, it will be interesting to observe the progress and long term results obtained by this method (Fig. 1).

## THE TYMPANIC GRAFT AND ITS APPLICATION TO THE VASCULAR BED

In the absence of infection the stability of the graft appears to be directly related to: 1) the thickness of the graft, 2) the preparation of the vascular bed, and 3) the application of the graft.

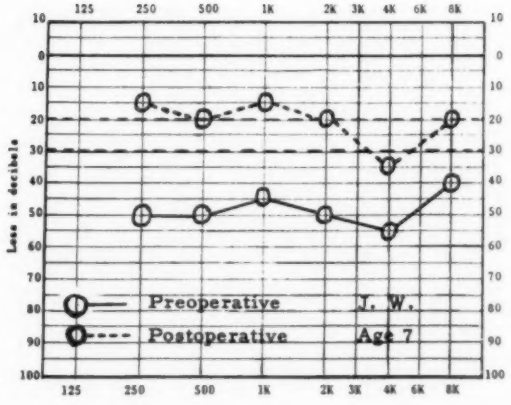


Fig. 3.—Postoperative result using polyethylene prosthesis for columella between graft and mobile footplate. Complete erosion of crura had occurred as a result of cholesteatoma.

1. *The Thickness of the Graft.* Our early experience with thin split thickness grafts[14] indicates that thin grafts almost universally slough. If a graft is to survive when bridged across the cavity of the middle ear it must contain the so-called collateral circulation afforded by the deep and superficial branching arterioles which run parallel to the surface of the skin. The graft must be at least ¾ split thickness in order to include these anastomosing vessels. Recent experience indicates that full thickness grafts may be more successful than the thick split thickness grafts (Fig. 2).

2. *The Preparation of the Vascular Bed.* The tympanic remnant (excluding calcareous plaques) and the adjacent canal wall are available for preparation as a graft bed. We believe the vascular bed should include an area surrounding the defect of 2 to 4 mm anteriorly, inferiorly and superiorly and 4 to 6 mm posteriorly. All remnants of squamous epithelium must be removed from the bed to which the graft is applied if a cholesteatoma or epithelial debris filled cyst is to be avoided between the bed and the graft. While Beickert[15] explains the etiology of these "flap cholesteatoma" by crypt or cyst formation in either epithelial folds or hair follicles, we believe that in

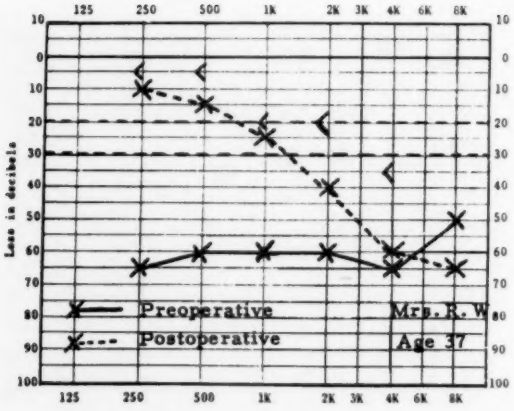


Fig. 4.—Myringoplasty with associated fixation of stapes due to tympanosclerosis. Postoperative result following repair of tympanic membrane and mobilization of stapes.

addition a certain percentage of them are caused by the incomplete removal of squamous epithelium from the vascular bed. Undetected squamous epithelium which has invaded the middle ear will likewise result in a surprisingly large cholesteatoma mass in a relatively short period of time when covered with a tympanic graft.

3. *The Application of the Graft.* If a graft is properly tailored to fit the area, excessive folding will be avoided and uniform and intimate contact with the vascular bed will be achieved. On the other hand, if a large graft of excessive volume is forced into the area, a reduced portion of the graft has proper contact with the available blood supply. Folding may tend to increase the possibility of "flap cholesteatoma." Adequate sag of the graft into the middle ear cavity should be anticipated so as to contact the full length of the long process of the malleus (or other ossicles in the advanced types of tympanoplasty). This sag not only allows for the normal concavity of the tympanic membrane but also affords adequate tissue to allow for contraction during the healing period. Contracture of a poorly applied graft may weaken or disrupt the contact of the new "tympanic membrane" with the ossicular chain.

Fig. 5.—Incision for posterior flap on posterior wall of external auditory canal wall. The flap is elevated to the level of the osteo-cartilaginous junction prior to postauricular incision.

Light packing around the periphery of the graft with cigarette paper and soft cotton balls affords adequate pressure to maintain the position of the graft. Tight packing compresses the capillaries in the graft and results in an increased tendency to cause central sloughs.

The skin on the adjacent canal wall will tend to extend under the graft and form "secondary cholesteatomas" unless it is carefully pulled back from under the edges of the graft. All canal flaps or skin edges in the canal are tailored so as to be in apposition with the graft or are allowed to overlap onto the graft rather than having the graft cover the canal skin. If the skin of the canal is allowed to

TABLE V

DETAILS OF 231 CONSECUTIVE TYMPANIC SKIN GRAFTS

1. Thick split thickness grafts
   161 total cases
   144 cases with two months or more follow-up
   32 grafts perforated (22%)

2. Full thickness grafts
   70 total cases
   48 cases with two months or more follow-up
   5 grafts perforated (10.4%)

remain under the edge of the graft, it will tend to grow under the graft, dissect it away from the tympanic remnant, and form cysts filled with epithelial debris (Table V).

ASSOCIATED PROBLEMS

1. *Erosion of the Crura of the Stapes.* Problems associated with erosion of the malleus and incus and disruption of the conduction mechanism have been adequately described previously.[8,10] The problem of erosion of the crura of the stapes with a remaining intact movable footplate may be overcome by the use of a polyethylene prosthesis between the graft and the footplate. Use of polyethylene which has been previously animal tested is recommended. Kley[16] adds a word of caution concerning the use of dental acrylic for this purpose due to the tendency of the acrylic prosthesis to be extruded through the graft.

Four of the six prostheses which we have used have remained in placed for periods of six to eighteen months to date. Extrusion of the prosthesis through the graft occurred in one case within six weeks of its application. It is believed that this tube was too long, creating so much pressure on the graft that a local slough occurred at the point of contact. Another prosthesis was displaced from its position and was found in the round window area at time of reoperation (Fig. 3).

2. *Tympanosclerosis.* Zöllner and Beck[17] described tympanosclerosis as "a deposit of amyloid-like material or frozen sugar" in the middle ear or epitympanic area in a small percentage of patients who have had chronic middle ear disease in childhood and tendencies toward allergic reactions. They believe that the process originates

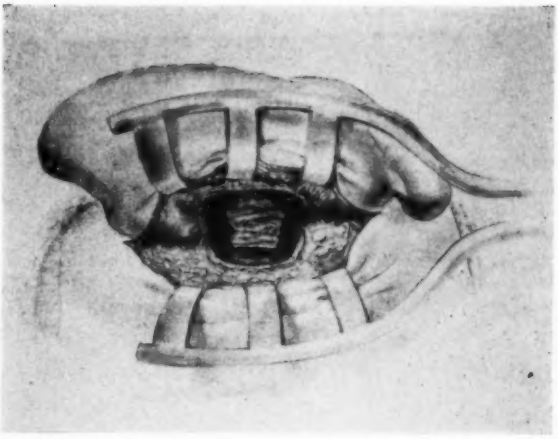

Fig. 6.—Postauricular incision and retraction of ear anteriorly revealing the posterior flap from the external auditory canal.

in the mucous membrane and that the calcareous plaque in the tympanic membrane may be the earliest visible sign of tympanosclerosis. It may be present in the middle ear or epitympanum without being present in the tympanic membrane. The process is usually not in continuity with bone but is separated with a thin membrane or fibrous tissue from the ossicles or the labyrinthine bone. This factor allows the material to be shelled away from the involved structure. The process can involve the ossicles, tympanic membrane, windows and, in rare cases, the whole air-containing space of the middle ear. They state that calcium deposits in the annular ligament of the stapes are a more common cause for a stapedial fixation than are adhesive processes (Fig. 4).

We have encountered definite tympanosclerosis in the middle ear and epitympanum in eleven cases in our series. In eight of these cases, it was possible to strip the tympanosclerotic bone away and allow for mobilization of the ossicles or to break the fixating process when the stapes alone was involved. In several other cases fixation of the stapes was found to be due to a definite otosclerotic focus. These cases required stapes mobilization in addition to tympanic repair.

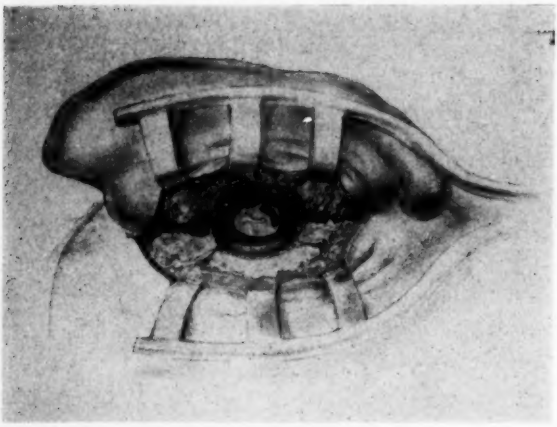

Fig. 7.—Posterior flap from the external auditory canal has been tucked up into the cartilaginous canal. Note incision line on bone of posterior canal wall outlining the former position of the posterior flap.

3. *Visibility in the Permeatal Approach to Myringoplasty.* The majority of cases in our myringoplasty series have been done through the external auditory canal. Visibility was gained by the use of combined anterior and posterior incisions in the external auditory canal which we have previously described[18] (Fig. 5). However, in our last 50 cases visibility has been considerably facilitated by the addition of a small postauricular incision. This addition to the previous technique was demonstrated by Bustamante[19] and associates in Mexico City. An elliptical incision is made in the postauricular sulcus centered over the level of the external auditory canal. The center of the incision is made sufficiently posterior to the sulcus to allow for adequate skin to be taken from the sulcus and posterior part of the pinna later for the graft. The skin of the anterior edge of the incision is then undermined until the cartilage of the pinna is reached. The cartilage is followed by sharp dissection into the external auditory canal. The flap previously elevated on the posterior wall of the canal is encountered and elevated into the lumen of the cartilaginous canal. The posterior flap from the canal is held in place by umbilical tape which is passed through the postauricular incision and out through

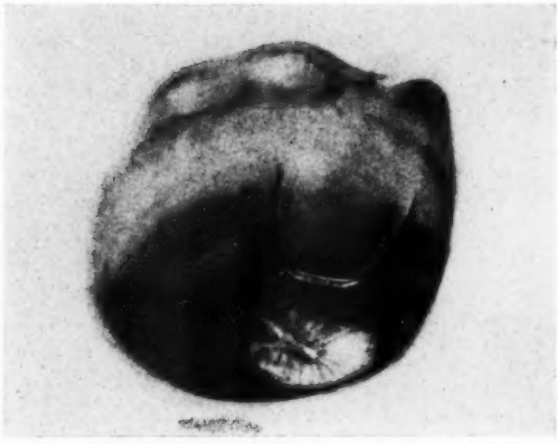

Fig. 8.—Details of U-shaped flap on anterior canal wall.

the cartilaginous canal. A postauricular retractor is then placed in the wound and the tympanic remnant is readily seen (Figs. 6 and 7). When the perforation is anterior or there is an overhanging anterior canal wall which obscures the angle between the tympanic remnant and the canal wall, an additional incision is necessary. This is a U-shaped incision, previously described,[18] which allows an anterior flap of skin to be elevated. Overhanging bone is removed with a sharp curette and adequate visualization of the total tympanic remnant is attained (Figs. 8 and 9).

4. *Postoperative Management.*

A. AntibioticTherapy: An appropriate antibiotic is administered in adequate doses for seven days postoperatively.

B. Removal of Packing: 1) Method of Removal: The cotton packs adjacent to the tympanic graft are removed by using a Day ear hook under the magnification of the otoscope. The cotton pledgets are gently teased away from the graft avoiding its displacement from the vascular bed or contact with the underlying ossicles. Loose cigarette paper strips used in packing are carefully removed with the same instrument. 2) Time of Removal: The packs are removed from myr-

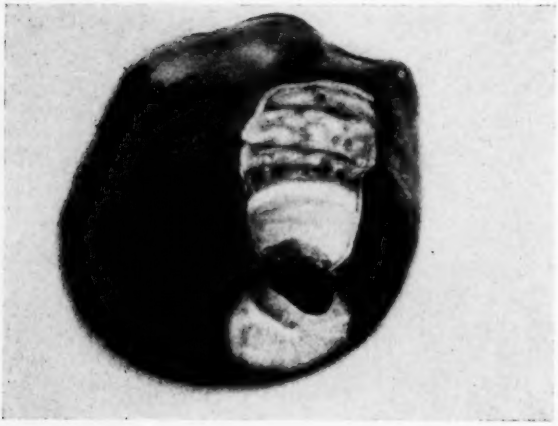

Fig. 9.—Overhanging bone of anterior wall has been removed with curettes after elevation of U-shaped flap.

ingoplasty cases in seven days and in advanced tympanoplasty cases in ten to twelve days.

C. Care of the Postoperative Cavity: Frequent careful cleansing of the cavity using sterile instruments and technique greatly facilitates early, complete healing. Specific antibiotic solutions are used locally as soon as the packing is removed. In the care of the cavity there may be two complicating factors, namely, the size of the cavity and delayed epidermization. The size of the cavity may be controlled, when necessary, by space obliterating techniques[20] at the time of surgery. Early healing of the mastoid cavity is facilitated by the application of secondary split thickness skin grafts two weeks postoperatively. If the tympanoplasty is done in two stages, the mastoid bowl is grafted two weeks after completion of the first stage. After control of the suppuration in the middle ear, the tympanic graft is applied as a second stage in the presence of a healed, clean mastoid cavity. These methods result in small, rapidly healed cavities completely covered with squamous epithelium in the majority of cases.

D. Late After-care: *Lappencholesteatom*[15] or "flap cholesteatoma" may form and be apparent in the tympanic graft as late as 12

to 24 months after surgery. The occurrence of these epithelial debris filled cysts should be suspected when the graft assumes an abnormal fullness in the involved area. Increased hyperemia of the area may be present due to localized infection in the graft. The hearing level is usually depressed when the vibrating area of the graft is involved. In our series we have had six such "flap cholesteatomas" of the central type, involving the vibrating portion of the drum with depression of hearing. In all of these cases it was necessary to remove the graft and apply a new tympanic graft.

Numerous small peripheral cysts have been encountered at the edge of the tympanic graft. Since these cysts are in an area overlying bone, they are readily apparent early in the formation. The peripheral type, since it occurs on the periphery of the graft, usually does not destroy the graft as it can be easily evacuated by removal of the top half of the dome-shaped cyst.

SUMMARY

Basic problems involving the application of tympanoplasy techniques are discussed, namely, the preparation of the surgeon, control of suppuration and temporal bone pathology, clinical evaluation of the hearing impairment, problems of eustachian tube function, and problems of applying and maintaining the tympanic graft.

Associated problems are discussed such as the use of the polyethylene prosthesis as a columella between the graft and the mobile footplate, and tympanosclerosis. In addition, the problem of visibility during surgery in the permeatal approach to myringoplasty and the postoperative management of tympanoplasty cases are discussed.

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LXII

# THE SURGICAL TREATMENT OF FACIAL PARALYSIS AND TRAUMATIC CONDUCTIVE DEAFNESS IN FRACTURES OF THE TEMPORAL BONE

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MONTREAL, CANADA

In closed head injuries, a longitudinal fracture of the temporal bone is the most common cause of severe damage to the middle ear. Bleeding from the ear, traumatic conductive deafness, and facial paralysis are frequent complications of this type of fracture. The conductive deafness may be temporary or permanent, depending upon the degree of damage to the ossicular chain. The facial paralysis may recover spontaneously, but incomplete recovery, or permanent paralysis, has been reported in approximately 25% of untreated cases.[11,13,25] A method of surgical treatment designed a) to permit recovery of the facial nerve, and b) to restore the traumatic conductive deafness to a servicable hearing level, has been employed, in selected cases, for the past ten years. Four cases have been chosen to illustrate the problems involved in the surgical treatment of facial paralysis and traumatic deafness in fractures of the temporal bone.

## CLASSIFICATION OF FRACTURES OF THE TEMPORAL BONE

Fractures of the temporal bone may be longitudinal, unilateral or bilateral, transverse, or a combination of both.

The longitudinal fractures, parallel to the long axis of the petrous pyramid, are the most common. Grove[11] found approximately 23% of these were bilateral in his series of 146 cases. This type of fracture usually involves the floor of the middle cranial fossa, spares the bony

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capsule of the inner ear but frequently, if not always, damages the middle ear. The facial nerve may be damaged in the tympanic portion, distal to the geniculate ganglion. In rare cases, the nerve may be injured in the vertical portion.[13]

Transverse fractures are mainly posterior cranial fossa fractures. The bony capsule of the inner ear is broken perpendicular to the long axis of the petrous pyramid. The middle ear is usually spared but the facial nerve is more frequently, and more severely, damaged in this type of fracture.

Combined fractures, longitudinal and transverse, may occur, in which case the middle ear and inner ear may both be damaged. In the cases that survive such severe injuries, the facial nerve has been found to be compressed or severed at more than one site.

### LONGITUDINAL FRACTURES OF THE TEMPORAL BONE

A longitudinal fracture is usually due to a force applied to the temporoparietal region.[11] According to most authors, the course of a longitudinal fracture is typical. When it originates in the squama of the temporal bone (Fig. 1) it passes downwards through the roof of the external canal and the roof of the middle ear. A descending branch may also run into the temporomandibular joint. When the fracture originates in the parietal bone (Fig. 1) it usually involves the upper part of the mastoid process, then passes along the posterior and superior walls of the external canal and through the roof of the middle ear. In both types, the fracture turns from the vault into the base (Fig. 2), along the anterior aspect of the petrous pyramid towards the apex, to end in or near the foramen lacerum.[11] Ramadier and Causse (quoted by Kettel, 1950) drew attention to an uncommon type of fracture restricted to the mastoid process itself, which may open into the external canal and middle ear and involve the facial nerve in the vertical segment.

According to Grove, "the middle ear is always damaged" in longitudinal fractures. The tympanic membrane is frequently torn, with the discharge of blood or cerebrospinal fluid from the ear. Brunner, Voss and Ruttin[11] believe, however, that cerebrospinal otorrhea is more common in transverse fractures than in longitudinal fractures. The middle ear cavity may be filled with blood clot, edematous mucous membrane, and fragments of fractured bone. The dura overly-

ing the tegmen may be lacerated. The ossicular ligaments and articular capsules may be torn,[12] and the incus may be partly or completely disarticulated from the malleus or stapes, or both.[9,12] I believe that the resulting traumatic deafness is more often permanent than is generally recognized.

The otic capsule remains undamaged in longitudinal fractures, but "marked perilymphatic hemorrhage into the scala tympani may take place, particularly near the round window."[11] A high-tone nerve-sensory type of hearing loss may result from the concussion of the cochlea. The extravasated blood in the scala tympani may be absorbed completely, with an entire restitution of function, and in this the age of the patient plays a very large role. The younger the patient, the better the chance for functional recovery.[11]

Although the facial nerve is often spared,[11] facial paralysis has been reported in 10 to 18% of longitudinal fractures of the temporal bone.[13] Rowbotham was able to trace in detail the course of a fracture which led to paralysis in three cases, two at operation and one at autopsy. In each case the fracture ended in the facial canal distal to the geniculate ganglion[18] (Fig. 3). Ney,[17] Cawthorne,[3] Kettel,[13] Schulthess and Dubs,[20] Feinmesser,[9] etc., have all reported similar findings.

I have gained the impression, from the damage seen in six cases at operation, that the force of a longitudinal fracture spreads the inner plate of the skull downwards from the vault into the base and bursts against the strong otic capsule (Fig. 2) shattering all of the thin compact bone and bony trabeculae overlying the facial nerve, in the upper half of the tympanic portion (Fig. 4). The facial nerve may thus be stretched (Fig. 5), contused, swollen, and compressed by the impinging bone fragments. I have not seen a case where the facial nerve was severed in this region by a longitudinal fracture alone.

## TRANSVERSE FRACTURES OF THE TEMPORAL BONE

A transverse fracture of the temporal bone is usually the result of a force applied to the occipital or occipitomastoid regions.[11] These fractures show considerable variation in position and direction (Fig. 6). There are two main types: a) the internal, which cuts across the internal auditory meatus and shatters the cochlea (Fig. 7), and b) the external type which passes through the cochlea, vestibule and

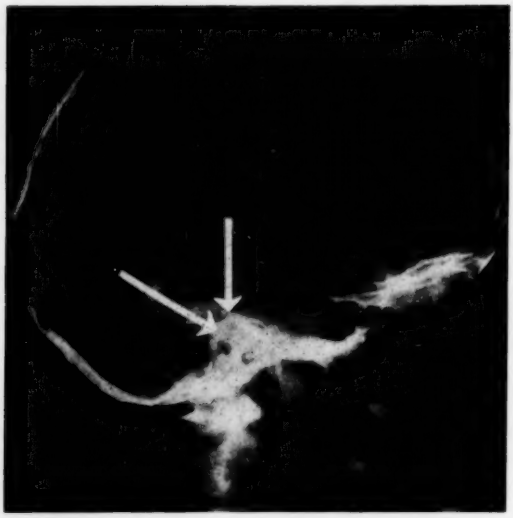

Fig. 1.—Longitudinal fractures arise in the squama of the temporal or in the parietal bone.

fallopian canal[11] (Fig. 8). In such cases there is an immediate facial paralysis, total loss of hearing and an absence of vestibular response. The middle ear may be spared, but if it is injured, the damage affects the medial wall, the eustachian tube, the knee of the facial nerve and the footplate of the stapes.[11] Transverse fractures rarely, if ever, cause a rupture of the drum and bleeding from the external canal, unless they are combined with longitudinal fractures.[11]

In contrast to the damage seen at operation in longitudinal fractures, in four cases of transverse fractures there was a complete disintegration of the promontory, with separation of the fractured bones through the lateral semicircular canal and fallopian canal. Fracture of the crura and luxation of the footplate of the stapes was observed in two cases. In one case there was almost complete section of the facial nerve by a dislocated sharp wedge-shaped bone fragment. In three cases there was complete section of the facial nerve with a turning of the proximal portion into the separated fracture line.

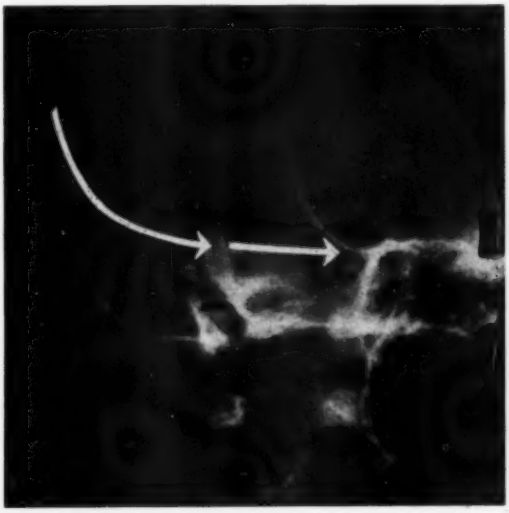

Fig. 2.—Longitudinal fractures arise in the vault and turn into the base of the skull.

## DEAFNESS IN FRACTURES OF THE TEMPORAL BONE

In longitudinal fractures Grove noted that in addition to the conductive factor, which must be due to damage of the middle ear, there is a perceptive factor which must be ascribed to an inner ear concussion occurring at the same time as the fracture.

In 69 cases with longitudinal fracture, Skoog[21] reported a conductive impairment in 65%, a perceptive or nerve loss in 22%, and a mixed type in 13%. In a follow-up seven to 13 years later, Skoog found normal hearing in 30%, conductive losses in 16%, and perceptive or mixed losses in 54%. This would still indicate permanent loss of a conductive or combined type in 70% of these cases. Schucknecht[19] also noted that "the occurrence of conduction deafness alone in the fractured ear is uncommon. Some degree of inner ear deafness is almost always associated with a conduction deafness."

The less severe conduction type hearing losses are partially reversible. The prognosis for the high-tone nerve-sensory type of

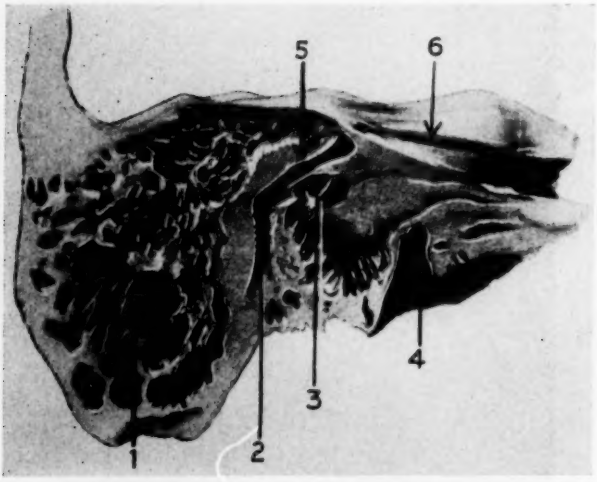


Fig. 3.—From Rowbotham (Acute Injures of the Head, with permission of the publishers, E. & S. Livingstone Ltd.) 1. Mastoid air cells. 2. Descending part of the facial canal. 3. Stapes. 4. Carotid canal. 5. The point at which fracture of facial canal usually occurs. 6. Groove for superior petrosal nerve.

impairment is less hopeful. Destruction of the cochlea and vestibule in transverse fractures produces total deafness and loss of vestibular function.

Grove concluded that "a traumatically produced hearing defect is just as apt to deteriorate further as it is to improve." Rowbotham agreed that the "prognosis is always doubtful in middle ear deafness."

### THE INCIDENCE AND PROGNOSIS OF FACIAL PARALYSIS

In closed head injuries, most authors agree that facial paralysis is always associated with a fracture of the temporal bone. The fractures are not always demonstrable in the roentgenograms, but it is important to remember that the fracture lines seen in x-ray films of the skull are in the restored position: at the moment of impact the fractured bones are widely separated and they return together, pro-

vided they are not held apart by soft tissues or gross displacement of the bones.

The facial nerve is more often paralyzed than any other motor nerve, perhaps because it has a longer course in a bony canal than has any other nerve in the body.[4] In a series of 1,550 consecutive head injuries reported by Turner,[24] the facial nerve was the second most commonly injured cranial nerve, being exceeded only by damage to the olfactory nerve.

Facial paralysis has been reported to occur in 10 to 18% of longitudinal fractures, and in 50% of transverse fractures of the temporal bone.[11,13] Davis[6] reported peripheral facial paralysis in 46% of middle fossa fractures.

In longitudinal fractures the facial nerve is most often damaged by compression, ischemia, etc., in the intratympanic portion, whereas in transverse fractures the nerve is usually lacerated or completely severed in the middle ear. In very severe injuries the nerve may be damaged at more than one site.

In longitudinal fractures the facial paralysis may be unilateral or bilateral, partial or complete, and the onset may be immediate or delayed. Immediate paralysis is usually complete, and is an indication of more severe damage to the nerve. In bilateral cases the onset may be immediate on one side, and delayed on the other.

In longitudinal fractures it is well known that spontaneous recovery of the facial paralysis occurs in the majority of cases. A careful review of the literature would suggest that complete recovery occurs in approximately 75%, incomplete or partial recovery in 15% and permanent paralysis in 10%.[11,13,25] These percentage figures are surprisingly consistent among most authors. Although it is difficult to obtain exact details in any large series of cases, it is certain that the first signs of recovery have been noted within a few days to three weeks in the vast majority that recover completely.[18,25]

In Turner's series of 70 cases of facial paralysis in closed head injuries, 36 were of immediate onset.[25] Complete spontaneous recovery occurred in 75%. Of those with complete recovery, 90% showed signs of recovery within a few days to three weeks. The remaining

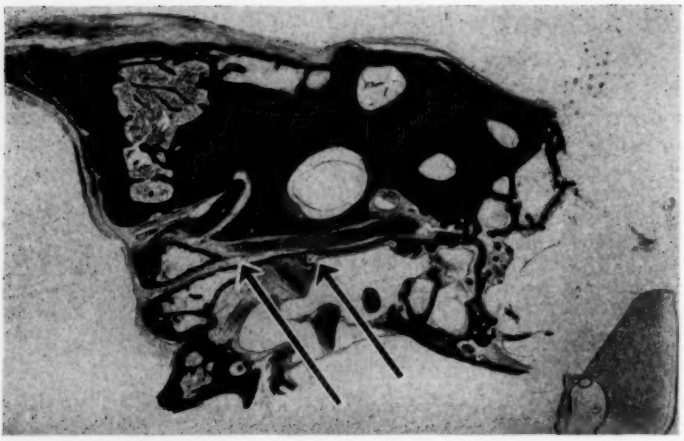

Fig. 4.—Horizontal section of the temporal bone. The arrows point to the facial canal, to the right and left of the processus cochleariformis.

10% began recovery within six to eight weeks and were complete in three months. In the cases that showed no improvement for three months, the recovery began slowly and in no case did normal facial movements return: 17% showed partial recovery with mass movements, and 8% resulted in permanent paralysis, a total of 25% that did not recover completely. In spite of these findings Turner stated that "my series provides no argument for operating unless there has been no recovery for at least six months after the injury, in which case exploration of the nerve in the facial canal might possibly be advisable."[25]

One would conclude, nevertheless, that if a case shows no evidence of recovery within three weeks the chances of complete recovery are considerably reduced, and after six to eight weeks are practically negligible. The recovery that occurs after a complete degeneration of the facial nerve is rarely complete.[5] Mass movements, or synkenesis, and spasms are more likely to occur in a nerve that has undergone complete Wallerian degeneration.

In general, the prognosis for the facial paralysis of delayed onset is better than for that of immediate onset; in delayed cases, the prog-

nosis is better for incomplete or partial palsy than for complete paralysis.[25] If infection supervenes, permanent paralysis is extremely common.[18,25]

## THE PRINCIPLE OF EXPOSURE AT THE SITE OF INJURY

Alt,[4] in 1908, was the first to report direct exposure and decompression of the facial nerve in two cases where the facial palsy occurred in the course of chronic suppurative otitis media with cholesteatoma. Stacke (1903), Kummel (quoted by Ballance and Duel),[1] Kennedy (1911), March (1900 and 1908), and Sydenham (1909) (quoted by Ballance and Duel)[1] all reported cases in which the facial nerve, injured during mastoid operations, was repaired at the site of injury.

Ney (1922) made a contribution to our understanding of the problems involved, that foreshadowed much of the work that was to follow. Ney[17] believed that "the only hope of restoring bilaterally co-ordinated emotional expression after a paralysis of the facial nerve lies in the restoration of the functional integrity of that nerve." His investigations convinced him that it was "possible and practical to expose and attack the facial nerve at a point where its injury is most common, namely, in its tympanic portion, where it passes between the fenestra ovalis and the lateral semicircular canal." He also believed that "injuries of the facial nerve, due to surgical trauma or fracture, involving the nerve in its tympanic course, are usually associated with a concomitant involvement of the air conducting apparatus, so that in the repair of these lesions (via the postauricular route) it is doubtful whether the exposure of the facial nerve in this region would materially increase the existing defective air conduction." Bunnell (1924)[2] and Martin (1931)[15] also advocated intratemporal repair of the facial nerve in traumatic facial paralysis.

The now classic experiments and investigations of Ballance and Duel (1932) led to the general acceptance of the fundamental surgical principle that "an injured (facial) nerve must be operated on at the site of injury." Ballance[1] insisted that "the aim of the surgeon is not only to cure the facial palsy, but also to preserve the hearing." In facial paralysis due to basal skull fractures, Ballance believed that the palsy is "permanent because of the inflammatory swelling the damaged nerve is so compressed by the bony tube within which it lies that regeneration and recovery of function are not possible." He

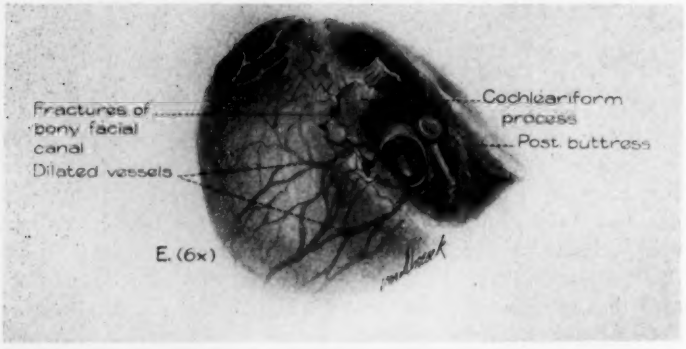


Fig. 5.—The damaged facial canal, between the lateral semicircular canal to the left and the stapes (artist's conception as seen at operation).

recommended decompression of the nerve immediately "with or without the use of a nerve graft," and concluded that the main difficulty to be overcome in these cases is localization of the site of fracture and determination of the exact place where the nerve is injured.[1]

In 1934 Duel found it remarkable that "although direct repair of the lesion in the injured (facial) nerve was attempted by many from 1900 to 1934, the repair by anastomosis with another nerve in the neck remained the operation of choice during all those years."[8]

It is more remarkable that 25 years later there is still a certain reluctance to explore and repair injuries to the facial nerve directly within the temporal bone. In facial paralysis due to longitudinal fractures of the temporal bone this attitude may be due in part a) to an incomplete knowledge of the pathology involved and b) to the fact that the majority of these facial palsies recover spontaneously. Kettel (1950)[13] cautioned, however, that "the prognosis of facial paralysis in closed head injuries is not so good as it is generally accepted to be and that this applies especially to the immediate paralysis." Cawthorne (1946)[3] stated that "although the number of cases in which the possibility of a surgically accessible lesion of the nerve has been appreciated is small, it is felt that skull fractures in which facial paralysis is accompanied by signs of damage to the ear,

particularly if the middle ear is affected, should be considered as possible instances of fracture involving the middle ear cleft and the facial nerve as it runs along its inner wall," and suggested that "exposure of the facial nerve-trunk at the site of the lesion in severe facial paralysis serves the double purpose of increasing appreciation of the causes and mechanism of this condition and of being the first step in the treatment of the lesion."[4]

Maxwell agreed that "definitive surgical treatment of facial paralysis due to basilar skull fracture is necessary in certain instances, and in these few properly selected cases it may be accomplished with gratifying results."[16] Tickle,[22] Fowler,[10] Collier,[5] Kettel,[13] Maxwell and Magielski,[16] Rowbotham,[18] Grove,[11] etc., have all subscribed to the same principle.

## INDICATIONS FOR OPERATION

In closed head injuries, Kettel believes that operation on the facial nerve is definitely indicated in some cases of facial paralysis, even if the number is limited.[13] From every point of view (the immediate and the delayed danger to life and the damage to cochlea and vestibular function) longitudinal fractures have a far better prognosis than the transverse, and quite the same applies to facial paralysis which may occur in connection with these skull fractures.[13]

Cawthorne[4] stressed that "it is important to know when the nerve should be exposed and when it should be left alone. To await spontaneous recovery which, because of the nature of the lesion cannot take place, may rob the patient of the chance of a good recovery; while to operate when spontaneous recovery is likely, may hinder the good work of Nature and encourage bad surgical judgment." Cawthorne concluded that "exploration of the nerve should be considered in cases of complete paralysis in which there is no sign (electrical or clinical) of returning function after a month, and where the lesion is thought to be surgically accessible"[4] (Fig. 9).

Rowbotham was of the opinion that "although theoretically routine decompression should be done in all cases, particularly the delayed ones, early operative interference is contraindicated because of the percentage of good spontaneous recoveries."[18] He advocated "exploration of the nerve regardless of the electrical reactions after three

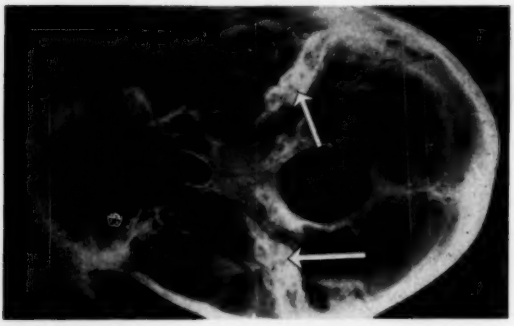

Fig. 6.—Transverse fractures of the temporal bone show considerable variation in position and direction.

months on those patients who have shown no improvement." Rowbotham, Turner[25] and others have shown that if infection supervenes operation is immediately indicated to prevent serious intracranial complications and permanent facial paralysis (especially if there is an associated cerebrospinal fluid otorrhea). An incomplete injury of the facial nerve may later lead to facial spasm, a condition equally as disabling, and probably more disfiguring than facial paralysis.[18]

Kettel (1950) "arrived at the conclusion that an exploration of the facial nerve should be done in cases of immediate paralysis as soon as the patient's general state of health permits it, provided that a final diagnosis of a severe lesion of the nerve in an accessible place can be arrived at." However, he finally concluded that "a decompression is indicated if after two months observation there is no sign of returning function."

It is agreed that there is great difficulty in selecting the proper cases for operation. The time of the onset of the facial paralysis is of first importance in deciding treatment, i.e., immediate or delayed. The syndromes described by Tschiassny[23] are excellent for localization of the lesion in the facial nerve, but examination of the patient may still leave some doubt as to the exact site. In estimating the severity of the lesion it is customary to rely on 1) the time of onset and the degree of paralysis, 2) on the electrical reactions of the nerve and

muscles found by applying the interrupted faradic and galvanic current to the nerve and muscles, and 3) on the electromyogram or strength duration curves. Lathrop[14] cautioned, however, "a positive electrical reaction obtained with faradic current or by electromyography suggests that the prognosis for spontaneous recovery is good, while a negative reaction merely indicates that the facial nerve is interrupted, but does not distinguish between physiologic and anatomic discontinuity of the nerve." In Lathrop's experience electromyography is not infallible. Strength duration curves may be more reliable but the early decision is still extremely difficult.

In view of the evidence that the first signs of recovery were noted within a few days to three weeks in 90% of the cases of immediate facial paralysis that recovered spontaneously following longitudinal fractures,[25] * it is obvious that there must be some significant difference in the pathology involved in the nerve in those that recover completely, as compared with those in which only partial recovery or permanent loss of function occurs.

I believe that the now classic experimental studies of Denny-Brown and Brenner[7] on peripheral nerve paralysis provide a significant answer to this problem. They confirmed that motor nerves offer less resistance to compression than do sensory nerves. The intermediate form of reaction of degeneration described by Erb (1876) was found to be due to the loss of myelin especially at the nodes of Ranvier.[7] Dejerine and Bernheim (quoted by Denny-Brown) reported a patient who had a *loss of motor conductivity with preservation of electrical excitability below the level of compression 25 days after paralysis due to pressure (during sleep) on the radial nerve.* At autopsy they found "only a granular (grénu) appearance of the myelin sheaths throughout the nerve, with vascular congestion at the supposed point of pressure."[7]

A British Committee on Nerve Injuries reported (1920)[7] that in pressure paralysis cases the "axis cylinders are damaged but Wallerian degeneration does not take place; they temporarily lose their normal conductivity but retain trophic power over the distal segment of the nerve" and "in a simple case the function of the nerve is restored within a few days or weeks."

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* The author's statement after reviewing Turner's series of 36 untreated cases where the exact time of recovery was stated.

Fig. 7.—Horizontal section of the temporal bone. Arrows indicate schematically the type of transverse fractures that cut across the internal auditory meatus.

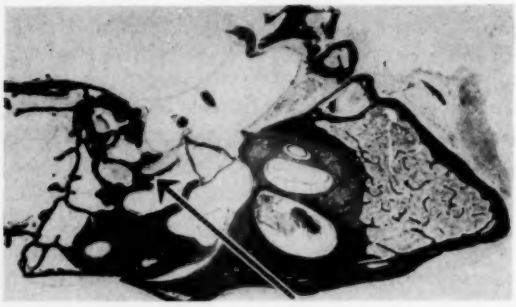


Fig. 8.—Horizontal section of the temporal bone. Arrows indicate the type of transverse fractures that cut across the cochlea, vestibule and fallopian canal.

Denny-Brown and Brenner conducted experiments directed toward a) determination of the relation of pressure to the onset and duration of paralysis, and b) establishment of the histologic nature of the Intermediate Form of partial degeneration described by Erb. They found that:

"The more transient type of motor paralysis, with sparing of sensation, is evidently that described by Erb in man, with what he

termed an 'intermediate type of reaction of degeneration,' for the electrical excitability of the nerve below the lesion is retained well beyond that of a degenerating nerve." Their histologic studies revealed that this is a disorder of conductivity of nerve without loss of anatomic continuity in the nerve fibers. "This lesion is of considerable interest. The damage takes the form of intermittent attenuations of the axis-cylinder and myelin sheath. The points of least resistance are the nodes of Ranvier and the region opposite the Schwann nucleus. The early observations (24 to 48 hours) on the lesion indicate an extensive disturbance of the protoplasm of the axis-cylinder, seen as swelling and vacuolation throughout the region subjected to compression. At this stage edema and lymphocytic infiltration have already appeared in the endoneurium. The emphasis then shifts to the myelin, which at the nodes of Ranvier becomes granular, fissured and vacuolated, with exposure of the bared or thinly covered axis-cylinder. Migrating histiocytes become filled with fat granules. These changes extend over a distance of 0.5 to 3 cm, beyond which normal structure is usually resumed. At the height of a severe lesion the non-medullated segments are as long as the remainder of the myelin. Beyond this stage of severity, in which the nerve has the appearance of alternating thin and thick fibers, the thin connecting axis cylinder presumably breaks. Once continuity is lost the distal segment degenerates, though the proximal part of the lesion has the characteristically widened nodes. *The stage of the lesion short of degeneration may persist as long as* 19 *days*, by which time recovery of conduction is beginning to occur. Most of the thin connecting links of axis-cylinder have then acquired a fresh, thin covering of myelin. Recovery of conduction is rapid and complete, but restoration of histologic structure appears to require more than two months. We are uncertain whether it is ever complete. Throughout this period the lesion is associated with obvious mesoblastic reaction and edema, both in the endoneurium and in the epineurium. The mesoblastic reaction is itself of great interest, for lymphocytes and macrophages are mobilized and edema has occurred within 24 hours. The mechanism for this reaction is a matter for speculation, but it is clear that there is usually no visible damage to the blood vessels."

Denny-Brown and Brenner in part concluded:

1. "With compression of short segments of peripheral nerve, great variation in rate and extent of impairment of conduction is

Fig. 9.—Complete peripheral facial paralysis on the right side with patient forcibly showing teeth and closing eyes.

caused by uneven pressure gradients in the nerve bundles, with consequent variation in the degree of ischemia due to escape of some small vessels.

2. "Under such conditions the onset of paralysis is in general more rapid the greater the applied pressure. This relationship is an expression of corresponding relative degrees of ischemia, and not a direct consequence of pressure on nerve fibers.

3. "The effect of pressure on conduction may be graded as of four degrees: a) nil; b) paralysis with rapid complete recovery on release of pressure; c) paralysis with delayed recovery without degeneration (intermediate type of pressure lesion), and d) complete anatomic lesion with degenerative phenomena. Attention is drawn to the third degree, which represents a lesion lasting from one to nineteen days, possibly longer, without signs of loss of excitability below the lesion and with preservation of gross sensation throughout."

In immediate facial paralysis following longitudinal fractures, it has been shown that spontaneous recovery may start within a few

days, and be complete in three weeks; or recovery may begin within three weeks and be complete in seven weeks.[25] In this type of fracture the facial paralysis is usually, if not always, due to "compression," rather than section, of the nerve in the tympanic portion. In cases showing no signs of recovery these findings would tend to favor early decompression; either before the end of three weeks to prevent degeneration, or before the end of seven weeks to permit regeneration.

If the associated traumatic conductive deafness suggests disarticulation of the ossicular chain, "the ultimate goal of surgical procedures on the facial nerve is (not only) physiologic restoration of its function"[14] but also restoration of the conductive deafness to a serviceable hearing level. Lathrop concluded that even when surgical treatment at the site of injury is delayed, "although the results of such procedures (on the facial nerve) are not perfect, in that varying degrees of mass motion obtain and fine emotional responses are not restored, they do serve to lift the burden of the grotesque half-mask which the patient suffering from paralysis of the face must bear and they accomplish this better than any other form of treatment at our command."

## THE SURGICAL TECHNIQUE

The surgical procedure that has been used in selected cases for the past ten years is illustrated in the accompanying sequence of drawings (Figs. 10 and 11).

The usual Shambaugh type of endaural incision is made (A) and (B) a modification of the usual fenestration type of meatal incision provides a cuff of external canal attached to the tympanic membrane posteriorly which is used in the final stages to close off the middle ear and permit the drum to be displaced inwards onto the head of the stapes. An atticotomy is then performed (C) exposing the heads of the ossicles. The disarticulated incus is then removed (D), the head of the malleus is amputated and the traumatic debris removed from the attic and middle ear. Under magnification, with the Zeiss operating microscope, the details of the damage to the facial nerve (E) can be assessed and appropriate measures taken to expose the facial nerve from the geniculate ganglion (F) down to the pyramidal eminence, or to the lower end of the lateral semicircular canal. When the facial nerve has been thoroughly exposed, a special curved sickle

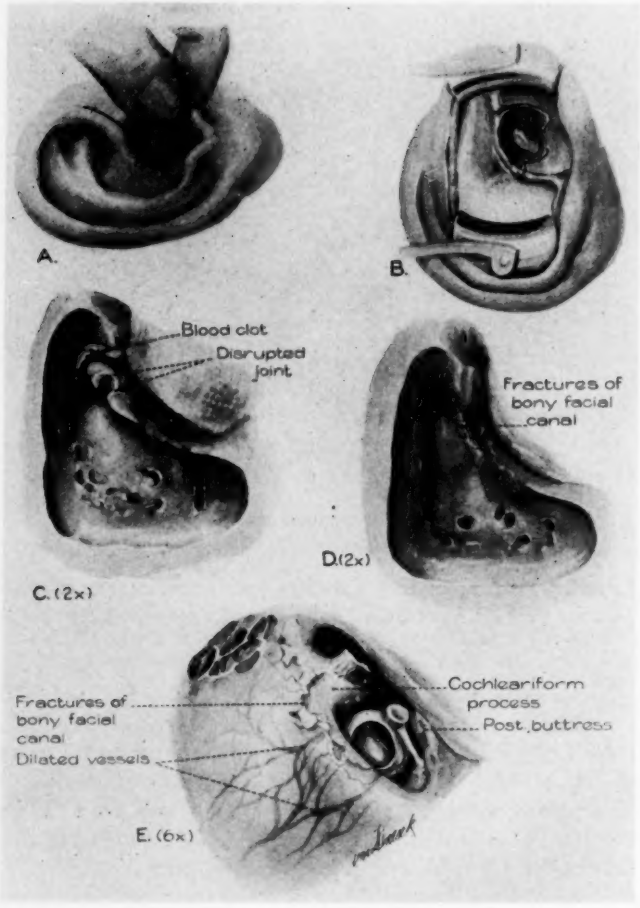



Fig. 10.—(See Surgical Technique)

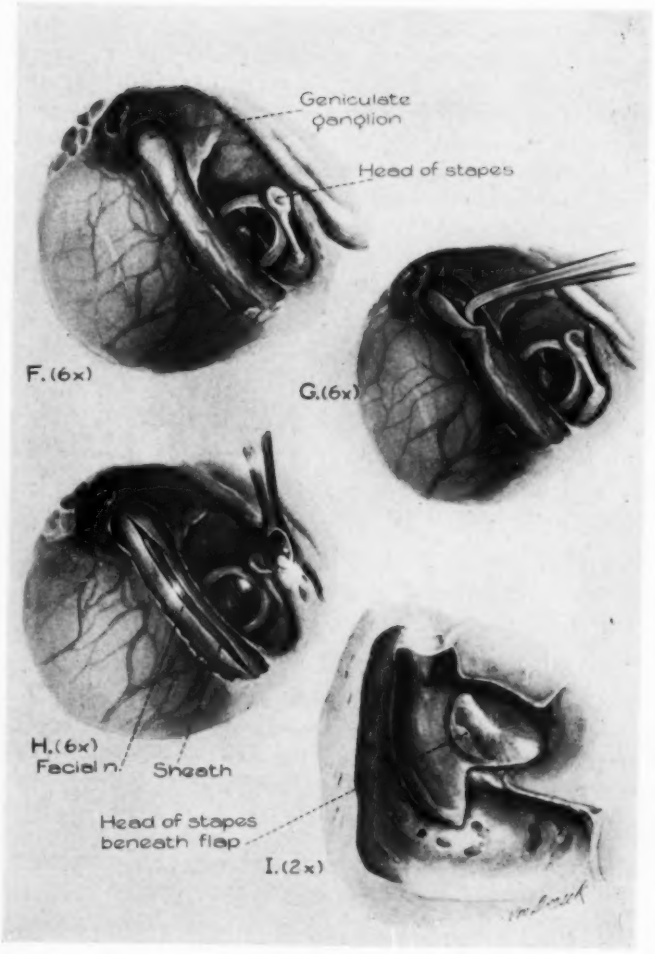



Fig. 11.—(See Surgical Technique)

knife (G) is used to incise the nerve sheath from above downwards, usually on the posterior surface. The posterior buttress is then removed (H) sufficiently to permit displacement of the tympanic membrane and attached meatal flap downwards over the head of the stapes, so that this prepared flap can close off the attic and middle ear from the mastoid space (I), i.e., a myringo-stapedio-pexy. Skin grafts may then be used to cover the facial ridge and mastoid bowl. The tympano-meatal flap and skin grafts are then covered with thin silk or nylon with a thread attached to permit easy removal at a later date, and the cavity is packed very lightly with plastic sponges soaked in Bacitracin and Chloromycetin. The packs are all removed on the seventh to tenth day following operation, and cleaning of the mastoid cavity is kept to an absolute minimum.

## ILLUSTRATIVE CASES AND COMMENTS

CASE 1. Mr. E.T., age 22 years, 1949.

Patient fell from a trestle and struck the ice twelve feet below with his head and shoulder. He was unconscious and had bleeding from the right ear. Admitted within two hours to the Montreal Neurological Institute, December 7, 1949.

*Diagnosis.* Fractured skull, clavicle, and transverse processes of C-7 and D-1. Question of immediate incomplete right facial paralysis. Left frontotemporal cerebral contusion and subarachnoid hemorrhage.

*X-rays.* A branched longitudinal fracture of the right temporal bone arising in the squama, the posterior branch entered the roof of the external auditory canal, and the anterior branch entered the temporomandibular joint. Right mastoid antrum and cells were airless.

*Progress.* Within 24 to 48 hours the patient had a complete right peripheral facial paralysis, with loss of taste on the right anterior two-thirds of the tongue.

December 12 and 13, 1949: Two generalized right-sided seizures with temporary nominal aphasia. Patient is right-handed.

December 28, 1949: Ear, nose and throat consultation: Both drums intact, right diffusely inflamed. Audiogram: A moderate

conductive hearing loss in right ear with a combined low tone and high tone loss, with relative preservation of middle tones( 1000 and 2000 c.p.s.) (Fig. 13). No spontaneous nystagmus. Vestibular tests: Normal responses on both sides. Facial nerve was considered to be involved distal to the geniculate ganglion, with normal tearing, and decompression was recommended.

December 29, 1949: Electromyogram showed no response to faradic stimulation, using more than 30 volts; galvanic stimulation gave a sluggish response.

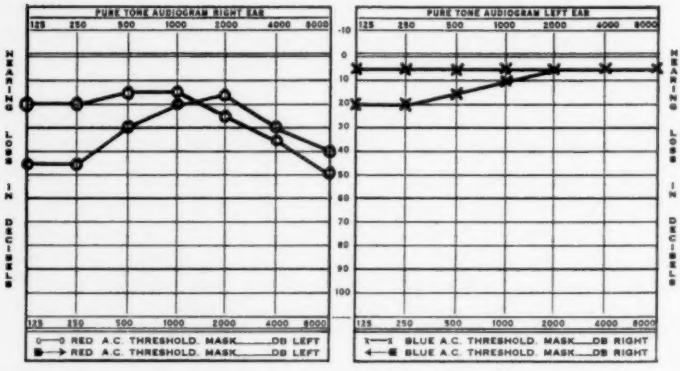
January 11, 1950: No faradic responses on right side using more than 30 volts and a significant decrease in galvanic response suggesting further degeneration of the facial nerve.

*Operation.* January 18, 1950: Forty-two days after possibly delayed onset of facial paralysis. Fracture line visualized running vertically down through the squama along the middle of the roof of the external canal, across the roof of the middle ear and into the floor of the middle fossa, anterior to the geniculate ganglion. Incus was removed and head of malleus amputated in order to expose the damaged portion of the facial nerve. Bone fragments, organized blood clots and swollen irregular masses of mucous membrane covering the course of the facial nerve were removed with the impinging fragments of the bony covering of the fallopian canal. The nerve from the region of the geniculate ganglion down to the lower limit of the lateral semicircular canal appeared to be swollen, and when the sheath was incised the nerve fibers bulged very definitely. In view of this the facial ridge was lowered and the upper portion of the vertical part of the facial nerve was decompressed. This part of the nerve appeared to be normal. The prepared skin flap was turned up to close off the attic, mastoid antrum and middle ear cavity: a myringo-stapedio-pexy was performed. The mastoid cavity was packed in the usual manner (see Surgical Technique).

*Results.* Definite evidence of recovery was first noted by the tenth day following decompression. The patient was given physiotherapy with massage and galvanic stimulation.

May 8, 1950: Electromyogram reported "a very marked improvement in the innervation of the right facial musculature."

Fig. 12.—Case 1. Mr. E.T. Decompression of right facial nerve 42 days after injury, 1950. (Photo 1959)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PURE TONE AUDIOGRAM LEFT EAR
HEARING LOSS IN DECIBELS
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-10 0 10 20 30 40 50 60 70 80 90 100
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●→ RED A.C. THRESHOLD. MASK____DB LEFT
X—X BLUE A.C. THRESHOLD. MASK____DB RIGHT
←E BLUE A.C. THRESHOLD. MASK____DB RIGHT

Fig. 13.—Case 1. Mr. E.T. Lower curves before operation, December 28, 1949. Upper curves, March 1959.

March, 1959: Very good recovery of facial movements, with servicable hearing in right ear (Figs. 12 and 13).

*Comment.* The immediate right facial paralysis was not complete for 24 to 48 hours. The associated conductive hearing loss suggested damage to, but not disarticulation of the ossicular chain. The electromyogram revealed no response to direct stimulation. Course of longitudinal fracture confirmed at operation six weeks after the injury: the facial nerve was still compressed by bone fragments, etc. Operation was recommended to permit regeneration of the nerve, and with the hope of improving the conductive hearing loss. The recovery of facial movements and restoration of hearing appears to be satisfactory.

CASE 2. Mr. R.J., age 29 years, 1956.

On January 26, 1956, a cut log slipped off an icy chute, struck the patient on the left forehead and crushed him to the ground. He was not unconscious. He had marked swelling and ecchymosis of the face and an immediate left peripheral facial paralysis, with bleeding from both ears, the nose and throat. There was a cerebrospinal fluid leak from the left side of the nose and a purulent discharge from the left ear, when he was transferred to the Montreal Neurological Institute, February 8, 1956.

*Diagnosis.* Fractured skull, with bilateral longitudinal fracture of the temporal bones. Fracture of right radius with separation of right acromioclavicular joint. Traumatic left peripheral facial paralysis with otitis media. Impaired hearing in left ear.

*X-rays.* Skull: Bilateral separation of the lamboid sutures with bilateral temporal fractures involving the mastoid air cells and bilateral fractures of the middle fossae. The mastoid air cells on both sides were filled with blood clot, cerebrospinal fluid or pus. The right sphenoid sinus was dense. There was an oblique longitudinal fracture arising in the postero-inferior part of the left parietal bone, extending down into the left temporo-mandibular joint. There was also a separation of the suture between the greater wing of the sphenoid on the left side and the adjacent petrous pyramid.

February 10, 1956: Ear, nose and throat consultation: Right ear canal clear, healing perforation of the right drum. Left canal

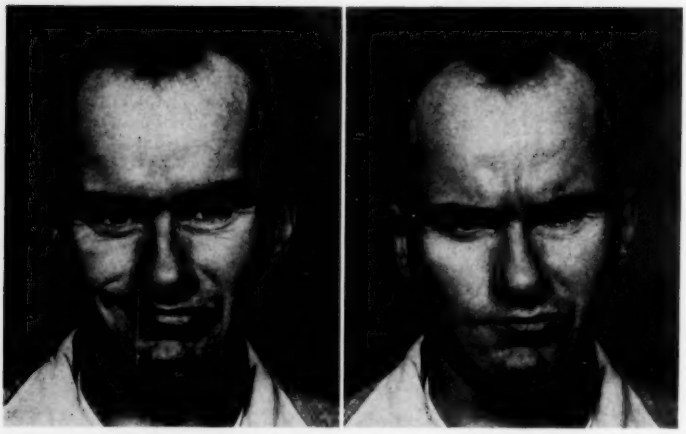


Fig. 14.—Case 2. Mr. R.J. Decompression 17 days after immediate left facial paralysis, with acute otitis media, 1956. (Photo 1958)

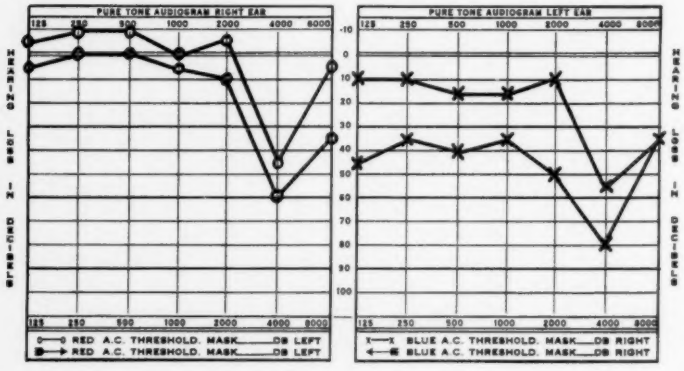

PURE TONE AUDIOGRAM RIGHT EAR
PURE TONE AUDIOGRAM LEFT EAR
125 250 500 1000 2000 4000 8000
HEARING LOSS IN DECIBELS
RED A.C. THRESHOLD. MASK____DB LEFT
RED A.C. THRESHOLD. MASK____DB LEFT
BLUE A.C. THRESHOLD. MASK____DB RIGHT
BLUE A.C. THRESHOLD. MASK____DB RIGHT

Fig. 15.—Case 2. Lower curves before operation February 10, 1956. Upper curves August 22, 1958.

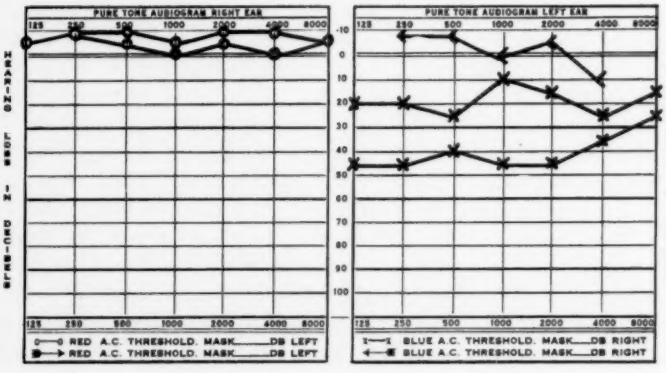
filled with purulent discharge coming from the attic region. Bacteriology reported staphylococcus pyogenes, insensitive to penicillin. Audiogram shows a bilateral high-tone nerve-sensory loss (Fig. 15), with a low-tone conductive loss in the left ear with an average loss for speech frequencies of 42 db. Vestibular test responses were normal on both sides. No other neurological disturbances.

In view of the acute purulent otitis media on the left side with the left facial paralysis and moderately severe traumatic conductive hearing loss, decompression of the facial nerve with plastic reconstruction of the left middle ear was recommended.

*Operation.* February 12, 1956: An endaural incision and atticotomy were performed seventeen days after immediate onset of facial paralysis. A fracture line was seen running down through the squama, along the roof of the external canal and across the tegmen tympani. Several fractured fragments of the anterior portion of the tympanic plate came away with ease. When the attic was exposed the ossicles were found to be embedded in a mass of ecchymotic and edematous mucous membrane, organizing blood clots and loose fragments of bone. The incus and head of the malleus were found to be disarticulated and the handle of the malleus was almost completely evulsed from its pocket in the tympanic membrane. The tendon of the tensor tympani was cut allowing amputation of the head and part of the handle of the malleus. The incus was removed, thus permitting proper exposure of the facial nerve in the upper part of the tympanic cavity. The fractured processus cochleariformis was removed, with the tensor tympanic muscle. The facial nerve was compressed just below the geniculate ganglion by the surrounding fragmented bony trabeculae and fractured tegmen tympani. The sheath of the facial nerve appeared to be ecchymotic for a distance of about 4 mm. There was a large dilated vein running along the upper surface of the sheath. When the sheath was incised the nerve fibers bulged through the incision immediately. The drum was freed in the posterior half from the tympanic sulcus and pressed against the roughened head of the stapes. The tympanomeatal flap was then turned up into the attic and mastoid antrum. The facial ridge and mastoid cavity were covered with a skin graft, taken from the leg. The cavity was treated in the usual manner.

*Results.* Some recovery of movement of the muscles around the left eye were noted within 24 hours. These disappeared within 24 hours

Fig. 16.—Case 3. Miss J.G. Decompression of left facial nerve 53 days after injury, 1955. (Photo 1958)


PURE TONE AUDIOGRAM RIGHT EAR
PURE TONE AUDIOGRAM LEFT EAR
HEARING LOSS IN DECIBELS
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-10 0 10 20 30 40 50 60 70 80 90 100
RED A.C. THRESHOLD. MASK____DB LEFT
RED A.C. THRESHOLD. MASK____DB LEFT
BLUE A.C. THRESHOLD. MASK____DB RIGHT
BLUE A.C. THRESHOLD. MASK____DB RIGHT

Fig. 17.—Case 3. Lower curves before operation, 1955. Upper curves September 15, 1958.

and reappeared in about 14 days. Patient received regular physiotherapy.

February 24, 1956: Electromyogram: "Evidence of progressive recovery of left facial muscles, which is evidence for regeneration of the left facial nerve."

June 11, 1956: A strength duration curve showed good recovery for the corrugator frontalis, orbicularis oculi and mentalis. There is still some failure of recovery of the risorius orbicularis oris and levator nari.

June 11, 1956: Audiogram showed a bilateral high-tone hearing loss with an average loss for speech frequencies in the left ear of 18 db. Audiogram: August 22, 1958: Average A.C. loss for speech frequencies, 13 db in left. Bilateral high tone 4000 cps. dip persists (Fig. 15).

*Comments.* The left facial paralysis was of immediate onset. The conductive hearing loss was due in part to the general middle ear trauma and acute otitis media, but mainly to the disarticulated malleus and incus. The damage to the facial nerve was more severe than in Case 1. Facial decompression and myringo-stapedio-pexy were performed early (17 days—two days after admission) because of the acute suppuration and the lack of response to faradic stimulation. The hearing was restored satisfactorily. The recovery of the facial muscle (Fig. 14) movements was incomplete, with some synkenesis. The result, however, was considered "satisfactory" in view of the reported incidence of 75 to 100% permanent facial paralysis in infected fracture cases.

CASE 3. Miss J.G., age 10 years, 1955.

This child was injured when struck by a truck on October 17, 1955. She was admitted to the Montreal Neurological Institute a few hours later, semiconscious, with blood and possibly cerebrospinal fluid discharging from the left ear, bleeding from both sides of the nose, and a complete left peripheral facial paralysis and impaired hearing in the left ear.

*Neurological Examination.* Revealed a partial left VI nerve paresis, some weakness of the right arm and leg, bilateral absent

abdominal reflexes and a positive right Babinski. Complete left facial paralysis and loss of taste in the anterior two-thirds of the left side of the tongue.

*Electroencephalogram.* Indicated rather severe damage to the left temporal region and evidence for abnormality of the brain stem.

*X-rays.* October 17, 1955. A longitudinal fracture of the left temporoparietal region with cloudiness of the mastoid air cells, especially on the left side. Air was demonstrated in the basal cistern.

*Progress.* The patient remained semiconscious for several days after admission. She complained of severe and persistent pain in the left ear. Gradual improvement in all respects. Discharged November 11, 1955, and readmitted to the Royal Victoria Hospital December 8, 1955.

*Ear, Nose and Throat Examination.* December 8, 1955. Ear drums intact. Left drum ecchymotic. Conductive and perceptive hearing loss in left ear. Vestibular responses were normal on both sides. Nose and throat clear. Complete left peripheral facial paralysis. Decompression of left facial nerve and reconstruction of the left middle ear was recommended.

*Operation.* December 9, 1955. First Stage (53 days after injury). Postauricular incision, because of the persistent cloudiness of the mastoid air cells by x-ray. A definite fracture line was seen along the posterior canal wall, and across the roof of the middle ear. The middle ear was filled with bone fragments, organized blood clot and edematous mucous membrane. The incus was removed and the head of the malleus amputated. The traumatic debris was removed from the middle ear with the aid of the Zeiss Operating Microscope at 10 x magnification.

The bony wall of the fallopian canal was depressed and fractured from the point of entrance of the facial nerve into the middle ear downwards to the level of the pyramidal eminence. The facial nerve was decompressed and the ecchymotic sheath was incised. The nerve fibers bulged outwards, especially in the middle third of this portion.

The postauricular wound was closed, with a drainage tube into the mastoid cavity, to permit recovery of the traumatized middle ear contents.

*Operation.* December 20, 1955. Second Stage. Endaural incision, and atticotomy completed. A modified fenestration type of tympanomeatal flap was prepared, and a myringo-stapedio-pexy was performed. Cavity packed in the usual manner, after skin grafts were placed in the mastoid cavity.

*Progress.* The first signs of recovery of the left facial paralysis were noted approximately two weeks following decompression. After a temporary drop, hearing was restored to a serviceable level. The last audiogram obtained September 15, 1958, shows an average loss for the speech frequencies of 17 db (Fig. 17). The damage to the facial nerve was severe and complete recovery did not occur (Fig. 16). The incomplete recovery and mass movements might have been prevented if earlier decompression had been possible.

*Comments.* The slight movement of the left upper eyelid noted after the patient regained complete consciousness was misinterpreted as evidence of early recovery of the left peripheral facial paralysis. The levator palpebrae superioris is supplied by the oculomotor (III cranial) nerve. Decompression of the facial nerve was delayed, as a result, until after seven weeks.

CASE 4. Mr. R.P., age 37 years, 1953.

This patient was injured in an automobile accident December 22, 1953. He had a closed head injury with a skull fracture and was unconscious for an indefinite period of time. There was an immediate left peripheral facial paralysis associated with bleeding from the left ear, and loss of the sense of taste on the left anterior two-thirds of the tongue. The latter was noted after his transfer to the Montreal Neurological Institute on December 29, 1953. He had marked swelling and ecchymosis above the right eye, and lower half of the left side of the face.

*X-rays.* December 31, 1953: Showed a fracture of the left parietotemporal bones extending into the upper part of the left mastoid process. There was a suggestion that the fracture ran very close

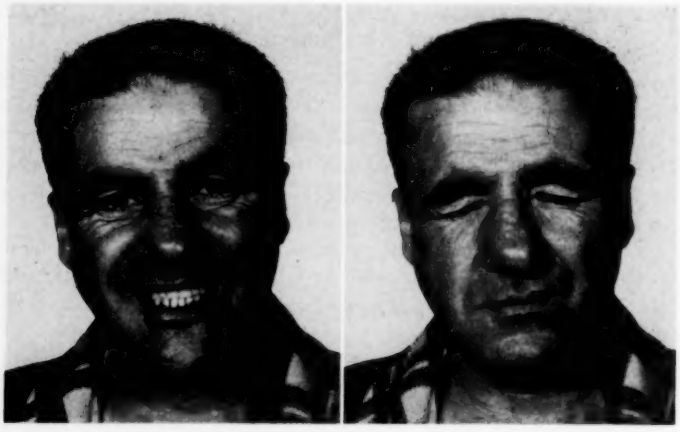

Fig. 18.—Case 4. Mr. R.P. Decompression of left facial nerve (vertical segment only) 25 days after injury, 1954. (Photo 1956)

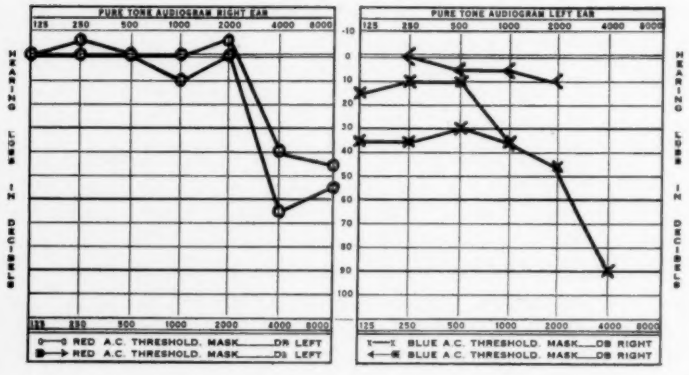
PURE TONE AUDIOGRAM RIGHT EAR
PURE TONE AUDIOGRAM LEFT EAR
HEARING LOSS IN DECIBELS
125 250 500 1000 2000 4000 8000
RED A.C. THRESHOLD. MASK____DB LEFT
BLUE A.C. THRESHOLD. MASK____DB RIGHT

Fig. 19.—Case 4. Upper A.C. curve for left ear before decompression of vertical segment of facial nerve. B.C. and lower A.C. curve, left, 1956.

to or through the vertical part of the left fallopian canal near the stylomastoid foramen.

*Ear, Nose and Throat Examination.* December 30, 1953: Right ear canal clear, drum normal. Left canal contained dried blood clot. Left drum intact, with hemotympanum. The nasal septum was dislocated anteriorly to the right. Marked ecchymosis at the base of the tongue on the right side.

*Audiogram.* December 30, 1953: Bilateral high-tone nerve-sensory hearing loss with a conductive loss in the left ear averaging 30 db for the speech frequencies by air conduction (Fig. 19).

Vestibular Tests: Normal responses in both ears.

*Strength Duration Curve.* January 11, 1954: Showed a typical curve of complete denervation. Electromyogram: January 15, 1954: Showed complete denervation with no electrical sign of functional recovery. "A spontaneous complete recovery seems unlikely."

*Operation.* January 16, 1954: (25 days after injury). Through a retro-auricular incision a complete left simple mastoidectomy was performed. The fracture line was seen in the squama of the temporal bone. It crossed the lateral wall of the mastoid antrum and entered the posterior canal wall in its upper third. The fracture ran downwards and forwards to the junction of the tympanic plate with the petrous, i.e., at the upper end of the vertical portion of the facial canal. The roof of the antrum (the floor of the middle fossa) was also found to be fractured, and there were fragments of bone and organized blood clot in this region. The facial nerve was found to be compressed by a large chip of bone which separated easily from the tympanic ring, just below the lower end of the semicircular canal. This was removed. The entire vertical portion of the facial nerve was exposed and the sheath incised, down to and beyond the stylomastoid foramen. The ossicles were not disturbed in the middle ear.

*Progress.* There was increased loss of hearing for two weeks after operation. The first signs of recovery of the facial nerve appeared approximately seven weeks after operation. The patient was not seen again until 1956 at which time there was slight asymmetry of

forced movements around the mouth and very minimal evidence of associated movements (Fig. 18).

*Comment.* This is an example of the difficulty that exists sometimes following a closed head injury, as to whether the facial paralysis was immediate or delayed in onset. In an unconscious patient with marked swelling of the face, it is most difficult to detect an immediate facial paralysis. In such cases its would appear to be in the best interests of the patient to regard the onset as immediate when such a doubt exists. The facial decompression was done 25 days following injury and it took approximately seven weeks for evidence of recovery. The end result is satisfactory, but proof again that a case in which the nerve has degenerated completely rarely permits perfect restoration of function. In this case the x-rays suggested that the facial nerve was involved in the lower end of the vertical position. In fact it was the upper end, and although the hearing appeared to be satisfactory shortly after operation, there is now a conductive component presumably due to partial fixation of the incus (Fig. 19). In such a case it might have been better to have decompressed the entire nerve from the geniculate ganglion down and to have restored the hearing by means of a myringo-stapedio-pexy.

## SUMMARY AND CONCLUSIONS

1. In closed head injuries, longitudinal fractures of the temporal bone, with damage to the middle ear, are more common than transverse fractures, which usually destroy the inner ear.

2. In longitudinal fractures a traumatic conductive deafness and facial paralysis may occur as complications. In this type of fracture the facial paralysis is most commonly due to a 'compression' of the surgically accessible tympanic portion of the facial nerve. The paralysis may be partial or complete, and the onset may be immediate or delayed. An immediate paralysis implies more serious damage to the facial nerve.

3. In transverse fractures of the petrous pyramid facial paralysis occurs more frequently, and in these the facial nerve is usually lacerated or completely sectioned in the tympanic portion.

4. In longitudinal fractures an associated traumatic conductive deafness, severe enough to suggest disarticulation of the ossicular

chain, demands consideration in the indications for the surgical treatment of these injuries.

5. A critical review of the reported clinical experience of others would suggest that, in longitudinal fractures of the temporal bone,

a) a facial paralysis may occur in approximately 10 to 18% of cases, and

b) spontaneous and complete recovery occurs in approximately 75% of the cases with an immediate onset,

c) signs of spontaneous recovery appear within a few days to three weeks in approximately 90%, and within three to seven weeks in the remaining 10% of the cases that recover completely,

d) the recovery that follows degeneration and impaired regeneration of the facial nerve is never complete. Mass movements and spasms of the facial musculature are common complications.

The experimental studies of Denny-Brown and Brenner tend to explain these clinical findings on the basis of a demyelinating "intermediate stage of degeneration" (described by Erb in man) that may exist at least 19 days, without showing the histologic changes of complete Wallerian degeneration.

6. The entire tympanic portion of the facial nerve may be decompressed, when indicated, whether there is a severe traumatic conductive deafness or not, provided appropriate measures are taken to restore the hearing to a serviceable level. It must be strongly emphasized, however, that this type of procedure should be undertaken only by those qualified, by experience or training, in the techniques of modern endaural reconstructive surgery, and with the aid of adequate magnification, such as that provided by the Zeiss Operating Microscope.

7. A surgical method of treatment designed a) to permit the recovery of function of the facial nerve, and b) to restore the traumatic conductive deafness to a serviceable hearing level, has been employed in a series of cases of longitudinal fracture of the temporal bone, for the past ten years. Four cases are reported to illustrate the problems involved and the results obtained.

8. The clinical and experimental evidence presented would tend to favor early decompression of the facial nerve in cases of facial paralysis that show no signs of recovery, either before the end of three weeks to prevent complete degeneration, or before the end of seven weeks to permit or facilitate regeneration.

3448 PEEL ST.

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I wish to express my sincere appreciation to Dr. W. V. Cone and Dr. Arthur Elvidge who extended to me the privilege of seeing the patients referred to in this paper at the Montreal Neurological Institute.

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# Scientific Papers of the American Broncho-Esophagological Association

LXIII

## PERFORATION OF THE ESOPHAGUS AFTER USE OF A DIGESTANT AGENT

### REPORT OF CASE AND EXPERIMENTAL STUDY

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PHILIP E. BERNATZ, M.D.
(by invitation)

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(by invitation)

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#### REPORT OF A CASE

A 27-year-old woman was brought to the Mayo Clinic desperately ill from an esophageal perforation with mediastinitis and empyema in both pleural spaces. Ten days earlier a bolus of meat had lodged in the cervical portion of her esophagus while she was eating her noon meal. Approximately three hours later a solution of caroid had been given to digest the meat and within two hours she had swallowed liquids satisfactorily. The next morning, approximately 12 hours after the ingestion of caroid, she had been discovered in a state of shock with subcutaneous emphysema in the neck. Cervical mediastinotomy and tracheotomy had been done and the administration of antibiotics had been started. During the ensuing two or three days empyema developed in each pleural cavity and bilateral intercostal drainage of these spaces with catheters had been established.

On transfer to this clinic ten days after her initial difficulty, little remained to be done except to assure adequate drainage from the mediastinotomy and both pleural spaces, administer proper antibiotics, and give sufficient supportive treatment with intravenously administered fluids and electrolytes. Micrococcus pyogenes, Pseudo-

From the Mayo Foundation, Rochester, Minnesota, a part of the Graduate School of the University of Minnesota.

Read at the Thirty-ninth Annual Meeting of the American Broncho-Esophagological Association, Hot Springs, Va., March 1959.

monas and Proteus were cultured from purulent material from all drainage sites. On the twelfth day of her illness, two days after her arrival at the clinic, massive hemorrhage suddenly developed from the cervical mediastinotomy and the patient died almost instantaneously.

Postmortem examination revealed that the fatal hemorrhage came from erosion through the wall of the common carotid artery. The cervical portion of the esophagus was completely destroyed for a distance of approximately two inches. There were fistulous passages into each pleural space from the cervical mediastinum.

## EXPERIMENTAL STUDY

In an attempt to determine the role caroid might have played in digesting and perforating the patient's esophagus we inserted a bolus of cooked meat perorally into the esophagus of each of several anesthetized dogs. The meat was tied to a whalebone staff and inserted into the esophagi of the dogs. After the meat was satisfactorily placed in each esophagus, the staff was fastened at the mouth so that the meat impaction would remain stationary. Caroid solution in the form of essence of caroid or half an ounce of caroid powder mixed with one ounce of water was introduced through a polyethylene catheter attached to the staff terminating at the upper level of the meat. The body of each dog was elevated approximately 25 degrees with the head above the feet.

Fourteen dogs were used in pairs (Table I). Initially the same size piece of meat was inserted into the esophagus of each of a pair of dogs, but only one dog received caroid. After three such pairs it soon became apparent that the meat alone produced no discernible damage to the esophagus, so controls were abandoned. Almost every dog receiving caroid showed some degree of damage to the esophageal wall with reddening of the mucosal wall and thickening of the wall at the site of the lodged bolus (Fig. 1). Microscopically epithelium was denuded in a patchy distribution without much inflammatory reaction. The meat impaction was friable and had about the same consistency as cooked fish. In addition the lungs of each dog receiving caroid showed the development of hemorrhagic edema which, in some instances, was sufficient to cause rapid death (Fig. 2).

## COMMENT

Caroid is a proprietary digestant containing papain which is a proteolytic enzyme obtained from the tropical papaw or melon tree, Carica papaya. In general its action resembles animal pepsin or tryp-

TABLE I

| DOG | CAROID, DOSE | FATE | ABNORMAL FINDINGS |
|---|---|---|---|
| 1 | 10 cc once; 3 cc 1 hr. later | Died in 3 hr. | Esophageal wall reddened, edematous; extreme hemorrhagic pulmonary edema |
| 2 | None; control for dog 1 | Sacrificed 3½ hr. | None |
| 3 | 5 cc hourly; 6 doses | Sacrificed 7 hr. | Esophagus reddened, edematous; moderate hemorrhagic pulmonary edema |
| 4 | None; control for dog 3 | Sacrificed 7 hr. | None |
| 5 | 5 cc hourly; 6 doses | Sacrificed 6½ hr. | Esophagus normal; extreme hemorrhagic pulmonary edema |
| 6 | None; control for dog 5 | Sacrificed 6½ hr. | None |
| 7 | 5 cc 30-minute intervals; 7 doses | Died 3¼ hr. | Esophagus reddened; extreme hemorrhagic pulmonary edema |
| 8 | 5 cc 30-minute intervals; 11 doses | Died 5¼ hr. | Esophagus reddened; extreme hemorrhagic pulmonary edema |
| 9 | 5 cc 30-minute intervals; 9 doses | Sacrificed 5½ hr. | Periesophageal edema; moderate hemorrhagic pulmonary edema |
| 10 | 5 cc 30-minute intervals; 9 doses | Sacrificed 5½ hr. | Periesophageal edema; slight hemorrhagic pulmonary edema |
| 11 | 5 cc 30-minute intervals; 4 doses | Sacrificed 16½ hr. (was about to die) | Esophageal wall hemorrhagic; extreme hemorrhagic pulmonary edema |
| 12 | 5 cc 30-minute intervals; 4 doses | Sacrificed 7 hr. (was about to die) | Esophageal wall hemorrhagic; extreme hemorrhagic pulmonary edema |
| 13 | 5 cc 15-minute intervals; 4 doses | Died 1 hr. | Esophageal wall hemorrhagic; extreme hemorrhagic pulmonary edema |
| 14 | 5 cc 15-minute intervals; 6 doses | Died 1¾ hr. | Esophageal wall hemorrhagic; extreme hemorrhagic pulmonary edema |

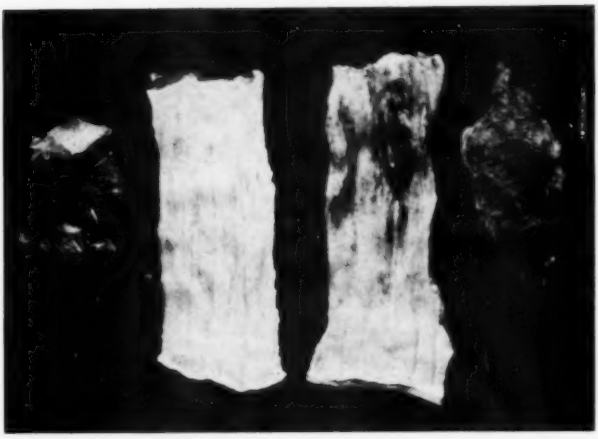

Fig. 1.—Bolus of meat and esophagus from control dog (left) and from dog 1 (right) which received caroid.

sin in its digestive action on proteins, and its medicinal use in this continent antedates the arrival of Columbus.

In 1945 Richardson[1] reported the use of this enzyme in the treatment of esophageal obstruction due to meat impaction. He narrated the histories of 16 patients whom he had treated with sips of a 5 per cent solution of papain successfully to digest a bolus of meat sufficiently to dislodge the obstruction in the esophagus. His treatment had failed in only one patient. Since then other reports[2-4] have appeared advocating the use of caroid for the treatment of meat impaction in the esophagus. We have not encountered a single report of an untoward reaction when caroid was used in this fashion. Tashiro and Schmidt[5] discovered no instance of harm to the gastrointestinal tract when papain was given. Supposedly this enzyme will not digest living, viable tissue except perhaps in a closed space. These authors demonstrated proteolytic damage when papain was injected intraperitoneally into rabbits.

We wondered whether an esophageal wall distended by a meat impaction might be sufficiently ischemic to allow the proteolytic action to attack the mucosa in addition to the cooked meat. We attempted to simulate clinical conditions in our experiment as closely

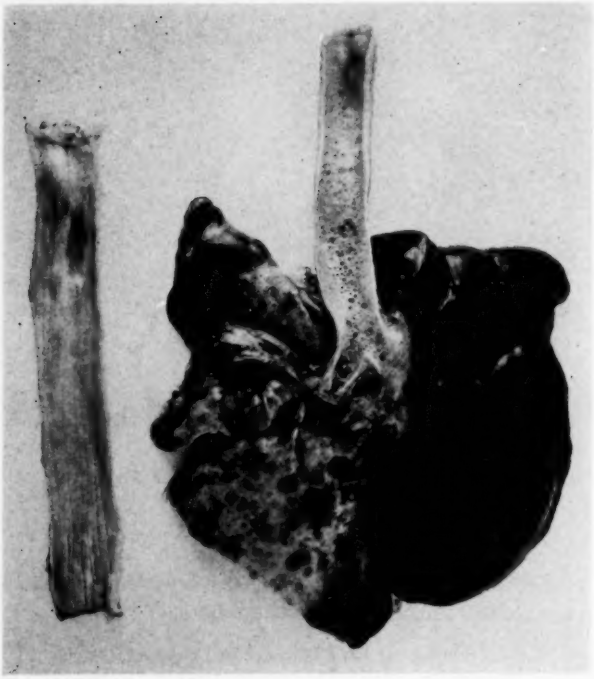

Fig. 2.—Lungs of dog 13 showing hemorrhagic pulmonary edema, more marked in the right or dependent lung.

as possible and, therefore, did not distend the esophagus of dogs with balloons or materials that would not invite the use of a protein digestant by a physician. In our opinion we have demonstrated that caroid is capable of damaging the wall of the esophagus. Even though we did not produce actual perforation of the esophagus, this is probably a matter of degree. We feel that prolonged contact of caroid with an ischemic esophageal wall is fraught with danger.

Godfrey and Miller[6] used several proteolytic enzymes on cooked meat and found that caroid was the most effective digesting agent. They thought crystalline papain was preferable, however, because it was sterile, whereas a gram-positive micrococcus was cultured from caroid. It is of interest to note that Micrococcus pyogenes was grown from the purulent drainage of our patient. We can only speculate about the role that this organism played in the course of her disease.

Hemorrhagic pulmonary edema was found in almost all dogs receiving caroid and was sufficient to cause the death of some. Our dogs were anesthetized and the pulmonary edema probably was due to aspiration of caroid into the tracheobronchial tree. In patients this complication probably would not be encountered because the person is usually advised to sip a solution and therefore must be awake with his cough reflex intact. The possibility of aspiration with esophageal obstruction is well recognized, however, and this serious pulmonary complication must be considered as a hazard.

## SUMMARY

The death of a 27-year-old, previously healthy woman from perforation of the esophagus after the use of a proprietary digestant (caroid) derived from Carica papaya for a meat impaction prompted us to investigate this proteolytic agent. Approximately 12 hours after the ingestion of caroid the patient experienced rapidly progressive, fulminating mediastinitis which terminated in perforation of the common carotid artery and sudden massive hemorrhage.

We conducted experiments on dogs and attempted to simulate clinical conditions by obstructing and distending the esophagus with a bolus of meat. Caroid was introduced just above the obstruction in some of the dogs. Definite damage to the esophageal wall was noted in those receiving this substance. We postulated that stretching and compression of the esophageal wall caused sufficient ischemia for the proteolytic enzyme (papain) in the digestant to act. Advanced hemorrhagic pulmonary edema causing death also was encountered.

Extreme caution in the use of caroid for treatment of meat impaction of the esophagus is urged.

MAYO CLINIC

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LXIV

# PULMONARY FUNCTION TESTS AS AN ADJUNCT IN BRONCHOLOGY

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In November of 1958, Rockey and his associates[1] presented a new method of producing bronchial drainage by a permanent tracheostomy in certain chronic debilitating chest diseases. The operative technique perfected by him is relatively simple, and consists basically in making a permanent window in the trachea with the formation of permanent skin valves, which permit the maintenance of normal continuity of the tracheo-bronchial tree, with the preservation of a normal voice.

The objectives of tracheal fenestration are three: 1) to remove tracheo-bronchial secretions in a selective fashion and at such times as the patient feels in need of this assistance; 2) to provide a substitute in whole or in part for faulty drainage and the impaired cough reflex attendant to some diseases; 3) to provide a simple, direct method of aerosolization and diminish the dead space when this is a factor in respiratory insufficiency.

## INDICATIONS

The types of patients who most benefit from the therapeutic steps cited above include two general classes of disease: 1) those individuals whose respiratory impediment is extra-pulmonary, as in diseases of the muscles of respiration, for example, poliomyelitis; 2) individuals with primary pulmonary disease. Both classes become candidates for tracheal fenestration when the basic incapacity lies in the patient's inability to spontaneously expel tracheo-bronchial secretions, an impaired cough reflex, and a diminished ventilatory capacity.

In the group of patients who have primary lung disease, these functional losses are most often seen in: 1) chronic pulmonary emphysema, generally of the "wet" variety secondary to asthma, a long history of smoking, or foreign body reaction of any type; 2) univer-

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sal bronchiectasis where the lung tissues are so completely diseased that excisional surgery is contra-indicated; 3) fibrocystic disease of the pancreas, with excessive pulmonary suppuration; 4) advanced and extensive nonsurgical tuberculosis; and 5) patients who have experienced respiratory insufficiency after excisional lung surgery or who might be expected to suffer such a deficit prior to surgery.

### CONTRA-INDICATIONS

Not all types of pulmonary cripples are candidates for tracheal fenestration, as a number of lung diseases are not problems from a standpoint of excessive secretions or loss of pulmonary elasticity. Chief among this group are: 1) those with pulmonary fibrosis, regardless of its cause; 2) pulmonary vascular disease or lung disease secondary to heart failure; 3) miscellaneous forms of localized functional loss such as phrenic nerve paralysis and thoracoplasty cripples.

Our experience with tracheostomy as a permanent means of alleviating respiratory disease began with that class of patients who did not have primary lung disease, but rather those who suffered from various forms of muscular impairment which limited pulmonary functions to a critical degree. This included approximately 150 cases of poliomyelitis in the 1952 Omaha epidemic.[2] Routine studies of the respiratory function were carried out, utilizing the Bennett Respirometer which gave direct data regarding vital capacity, tidal volume, minute volume (t.v. times the rate of respiration), maximum breathing capacity, and the inspiration-expiration volumes. Following these studies a bronchoscopy and tracheostomy were done. The tests were repeated at regular intervals and the measuerd improvement was found to parallel the clinical course.

These few tests proved of great value in an earlier selection of candidates for tracheotomy prior to the classical indications. Statistically, their use in the polio epidemic in Omaha resulted in an early bronchoscopic management and tracheotomy, with a marked decrease in the morbidity and mortality rate, being only .75 to 1.5 per cent, equalled only in Ann Arbor and Boston, whereas the mortality elsewhere varied between 5 and 10 per cent.

Because of the correlation between the data obtained from the above function studies and the clinical course of the patient, with Rockey's demonstration of the permanent tracheal fenestration benefits, we were interested in determining whether a similar relationship between the function tests and the clinical benefits of bronchoscopy

and tracheostomy could be demonstrated. To this end a group of patients thought to be ideal candidates for tracheal fenestration were selected, given the pulmonary function tests, bronchoscoped, and then re-evaluated by the pulmonary function tests and clinically. Bronchoscopy was selected, as it seemed the best method of producing, for a temporary period, those benefits which fenestration offered on a permanent basis. Before showing the results of this study, the criteria for candidate selection, which will become of increasing significance with popularization of the tracheal fenestration, will be presented.

Any patient with pulmonary insufficiency basically due to functional impairment caused by excessive tracheo-bronchial secretions and unable to expel them, is felt to be a potential candidate for tracheal fenestration.

The group of such patients studied by us was carefully evaluated clinically by history, physical examination, x-rays including fluoroscopy, and cardiac evaluation. Our object was an attempt to eliminate those individuals with excessive fibrosis or parenchymal damage which was not due to a failure in the mechanical aspects of respiration. These clinical methods were found to be by far the most rewarding, with the function studies principally of benefit in eliminating those patients where mixed pathology is present. Patients with such diseases as asthma, bronchiectasis, carcinoma, emphysema and fibrosis have been so studied. While some conditions, such as bronchiectasis, will apparently benefit from tracheal fenestration, we have limited this presentation to a summary of five advanced emphysema cases studied for tracheal fenestration.

These patients were studied with the following pulmonary function tests:

1. Minute volume
2. Tidal volume
3. Inspiratory capacity
4. Expiratory reserve
5. Vital capacity
6. Maximum breathing capacity
7. Maximum inspiratory pressure

8. Maximum expiratory pressure
9. Nitrogen meter
10. Functional residual capacity
11. Residual volume
12. Total lung capacity
13. Residual volume as percentage of total lung capacity.

TABLE I

SUMMARY OF FIVE REPRESENTATIVE ADVANCED EMPHYSEMA CASES STUDIED WITH PULMONARY FUNCTION TESTS FOR TRACHEAL FENESTRATION*

| PULMONARY FUNCTION TESTS | PREBRONCHOSCOPY | POSTBRONCHOSCOPY | POSTFENESTRATION |
|---|---|---|---|
| Minute Volume | 5.6 L. | 4.9 L. | 5.4 L. |
| Tidal Volume | 400 cc | 350 cc | 300 cc |
| Inspiratory Cap. | 755 cc | 1200 cc | 675 cc |
| Expiratory Res. | 800 cc | 500 cc | 1000 cc |
| Vital Capacity | 1575 cc | 1700 cc | 1675 cc |
| Max. Br. Cap. | 17.78 L./min. | 11.84 L./min. | 14.76 L./min. |
| Max. Insp. Pres. | without leak 90 cm/$H_2O$ with leak 30 cm/$H_2O$ | without leak 68 cm/$H_2O$ with leak 10 cm/$H_2O$ | without leak 40 cm/$H_2O$ with leak 40 cm/$H_2O$ |
| Max. Exp. Pres. | without leak 60 cm/$H_2O$ with leak 80 cm/$H_2O$ | without leak 60 cm/$H_2O$ with leak 28 cm/$H_2O$ | without leak 90 cm/$H_2O$ with leak 40 cm/$H_2O$ |
| Nitrogen Meter | Slope 11% in 500 cc (Normal less than 2%) | Slope 25% in 500 cc | Slope 15% in 500 cc |
| Functional Res. Cap. | 3.810 L. | 3.995 L. | 4.840 L. |
| Residual Volume | 3.010 L. | 3.455 L. | 3.840 L. |
| Total Lung Cap. | 4.585 L. | 5.080 L. | 5.515 L. |
| R. V. as % of T. L. C. | 66% (Predicted average normal is 29%) | 68% | 69.5% |

* Three have had the procedures. Two are pending at this writing. The symptomatic relief obtained is between Grade III and Grade IV.

All tests performed while patient was seated.

These tests are primarily directed toward establishing the mechanical efficiency of the tracheopulmonary apparatus and do not measure the deficits which result from vascular disease or the so-called capillary-alveolar block. After testing, each patient was bronchoscoped and a thorough tracheobronchial toilet was effected. The patient was then assessed as to his subjective feeling of relief and gross clinical improvement, such as his state of alertness, exercise tolerance, and freedom from cough. At the same time, the pre-operative pulmonary function tests were repeated and compared. The results were as indicated in Table I and Table II.

TABLE II

THESE PULMONARY FUNCTION TESTS SHOW:

A. PREBRONCHOSCOPY:
   1. Good respiratory effort - maximal pressures are higher
   2. Severe hyperinflation interfering with breathing - the large drop in inspiratory pressures with a small controlled leak
   3. A large residual volume
   4. Gas trapping
   5. Severe defect in gas distribution
   6. Reduction in vital capacity to one-half normal
   7. Severe reduction of maximal breathing capacity to one-fourth normal
   8. Impression from these pulmonary function tests: emphysema, Grade III - IV

B. POSTBRONCHOSCOPY:
   1. Severe defect in gas distribution by S.B.T., as prebronchoscopically
   2. Marked gas trapping as above
   3. About same values for vital capacity and functional residual capacity
   4. Greater loss of respiratory strength when measured with a leak indicates fatigue and explains decrease in maximum breathing capacity
   5. Because of this postbronchoscopic studies show but slight effect on patient

C. POSTFENESTRATION:
   1. All findings are about the same as the pre- and postbronchoscopic tests, but the symptomatic relief following bronchoscopy and tracheal fenestration on a clinically graded basis averages between Grade III and Grade IV.

From this summary of cases studied for this presentation, there was an excellent clinical response (Grade III - Grade IV) in three patients who have already had the tracheal fenestration, and on this basis an identical clinical result is anticipated for the other two candidates in this series. This summary does show, however, that this excellent clinical response was not paralleled by the pulmonary function studies, which were only slightly improved, unchanged, or worse than before. The explanation for this disparity requires further dis-

cussion of these tests, their benefits and limitations as an adjunct in bronchology.

The minute volume, tidal volume, inspiratory and expiratory capacity with the vital capacity and maximum breathing capacity have one feature in common. They are dependent on the patient's utmost co-operation and ability to reproduce his previous performance. This may be simple, but in the case of the respiratory cripple, it is akin to asking a maximum effort on several occasion during which interval much may have transpired both to improve or to impair the performance. For example, the amount of secretions, the presence of pneumonia, and the exhaustion of the accessory muscles of respiration. Even under the best of circumstances they are subject to a margin of error in excess of 20 per cent which makes them statistically invalid. In the cases of poliomyelitis this did not apply, as there was no lung disease but only an obstruction to the airway because of muscular weakness.

These tests are of definite qualitative significance, and are of great help in differentiating the type of lung disease, for example, emphysema versus fibrosis. The former is always characterized by an increased residual volume, and a decreased maximal breathing capacity, while fibrosis has a decreased residual volume and normal breathing capacity. Similarly in pulmonary heart and vascular disease, these tests are normal and easily rule out the unsuitable candidates for tracheal fenestration.

For these reasons we have found it practical and expedient in bronchology to limit the types of testing to six specific procedures which serve to delineate the type of lung disease without any attempt at the quantitations of these diseases. These test are:

1. Maximal breathing capacity
2. Vital capacity
3. Tidal volume
4. Inspiratory capacity
5. Expiratory capacity
6. Nitrogen single breath test

The last mentioned test, the nitrogen single breath test of Fowler, would appear to have more potential merit in bronchology than any single test previously proposed. Its basic principle is that if one

breathes room air, the expired gas is about 80 per cent nitrogen, 15 per cent oxygen, and 1 per cent to 2 per cent $CO_2$. If one then breathes oxygen and the expired gas is analyzed for nitrogen, the concentration of the element will decrease as a function of its dilution by the inhaled oxygen. For example, at the onset of inhalation a patient has 1500 cc lung volume which is 80 per cent N or 1200 cc N. If 500 cc of $O_2$ is added, the total gas is 2000 cc with 1200 cc N, 500 cc new $O_2$ and approximately 300 cc old $O_2$. Therefore nitrogen volume over total volume times 100 equals nitrogen concentration. If a series of measured amounts of $O_2$ are inhaled each time (500 cc $O_2$), the nitrogen concentration falls each time. The expired gas is continuously analyzed, and the slope is measured as an index of intrapulmonary mixing. The steeper this slope, the poorer the mixing and the greater the degree of loss of pulmonary elasticity, the surest index of emphysema. The benefits of the nitrogen single breath test are that it is simple, quantitative, and specific. The results of its use in a small series af adults with various types of pulmonary diseases are recorded in Table III.

TABLE III

INCREASE IN $N_2$ CONCENTRATION WITH SINGLE BREATH TESTS IN ADULTS WITH PULMONARY DISEASE:

| DIAGNOSIS | NUMBER OF PATIENTS | AVERAGE INCREASE |
|---|---|---|
| Asthma | 3 | 3.5 |
| Bronchiectasis | 5 | 4.7 |
| Carcinoma | 2 | 5.0 |
| Emphysema | 10 | 6.8 |
| Fibrosis | 5 | 3.6 |

## SUMMARY

The results as presented above led us to the following summation: 1) The subjective relief experienced by patients after bronchoscopy is not paralleled quantitatively in pulmonary function studies; 2) on the contrary, some of the most striking degrees of clinical improvement showed no improvement or poorer results on their subsequent pulmonary function tests; 3) repeated analysis of these tests led us to believe that their merit lies principally in diagnosing the nature of the disease, but is of no value in predicting the results of tracheal

fenestration when bronchoscopy is the pre-operative method of testing (attempting to simulate the results of tracheal fenestration by thorough pre-operative tracheobronchial aspiration); 4) it is our opinion that the pulmonary function tests are limited because: (a) they require an intense degree of co-operation on the part of the patient as in the case of maximum breathing capacity and timed vital capacity; and (b) in chronic respiratory insufficiency the disease varies from day to day (amount of secretions, presence of pneumonia) or from hour to hour, so that patients tested before bronchoscopy in the morning may show no change by the same testing in the afternoon, despite aspiration of great quantities of tracheobronchial secretions and despite the marked objective and subjective clinical improvement. The reason for this lies in the exhaustion of the accessory muscles of respiration, which is a constant factor in patients with respiratory insufficiency of all types; (c) changes in the blood pH, $CO_2$, $NO_2$ levels from day to day further preclude accurate comparisons by these tests; and (d) these tests are expensive, requiring elaborate equipment and personnel often lacking in institutions which are not large centers.

## CONCLUSIONS

In conclusion, the role of the above selected pulmonary function tests in our experience is found to be limited to the qualitative diagnosis in differentiation of various chest diseases, having little or no merit as a quantitative test with dependable results in any given individual. Because the number of tests available are numerous and complex, we further analyzed our data in an attempt to find the simplest test or combination of tests which would give the highest degree of accuracy. Our objective here was not to evolve a quantitative evaluation routine, but rather to establish a testing method to facilitate the diagnosis of the nature of the chest disease itself (emphysema, chronic fibrosis or heart disease). Six tests were selected and presented as the most practical adjunct to bronchology.

The discussion of the pulmonary function tests has been presented as an adjunct to bronchology in candidate selection for tracheal fenestration. While an analysis of our studies shows them to be of great value in establishing the nature of the disease process causing respiratory insufficiency, unfortunately they were found to be of no value, and can be indeed even misleading, as a means of pre-operatively testing these patients.

In conclusion, it is our considered opinion that bronchoscopy as a definitive pre-operative test is the best single means of anticipating

the results of tracheal fenestration. This method of carrying out thorough tracheobronchial aspiration has been found in our experience to be the best single means of anticipating the results of tracheal fenestration, with the patients' objective and subjective improvement being a far more accurate index of operability than even the selected pulmonary function tests which, as repeatedly pointed out above, at their present state of development are only an adjunct in bronchology.

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The author is indebted to Jerome P. Murphy, thoracic and cardiac surgeon, St. Joseph Hospital, Omaha, for his continued encouragement in adapting these tests to bronchology, and to A. W. Brody and staff, cardio-pulmonary laboratory, St. Joseph Hospital, Omaha, for their help and suggestions regarding these studies in bronchology.

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LXV

# THE MANAGEMENT OF ESOPHAGEAL VARICES IN CHILDREN BY INJECTION OF SCLEROSING AGENTS

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Hemorrhage from esophageal varices is a dreaded and frequently fatal complication of portal hypertension, or what really is hypervolemia in the portal venous system. Portal hypertension results from obstruction to the portal venous flow, either intrahepatic from disease in the liver itself, or extrahepatic (the so-called Banti's syndrome) from obstruction in the portal venous system. As a result of portal obstruction of either type, Butler[4] has stated that any or all of the veins of the esophagus may become varicose. However the esophageal varices do serve as one of the main collateral channels through which nature by-passes the obstruction and shunts blood flow from the portal to the systemic circulation. Butler has classified the esophageal veins as: 1) intrinsic, including subepithelial, submucous, and perforating; 2) extrinsic (or subserous) which are formed by the union of groups of perforating veins; and 3) vena comitantes of the vagal nerves, which run longitudinally in the adventitia of the esophagus. The varices in the subepithelial group of the esophagus are subject to severe hemorrhages. Hemorrhage may also occur from gastric varices. Kegaries[9] has reported the larger venous channels of the stomach are subserosal in position and therefore on the outer surface of the organ, less vulnerable to hemorrhage. However Learmonth[11] states that the submucous veins of the stomach as well may become varicose, but later than those of the esophagus.

The cause of spontaneous hemorrhage from esophageal varices has not been specifically established. No doubt there may be several

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factors, such as regurgitation of acid gastric contents, local injury by food, exertion, acute gastritis, and upper respiratory infections.

The first clinical signs of the presence of esophageal varices in the great majority of patients are either gross melena or massive hematemesis. Diagnosis of esophageal varices usually may be made by roentgenograms in which the varices present a typical beaded or necklace appearance. Esophagoscopy, however, provides a more accurate diagnostic procedure and at the same time the extent of the involvement and the state of the esophageal mucosa may be more satisfactorily evaluated. The appearance of esophageal varices through the esophagoscope is characteristic. They appear as bluish, balloon-like protrusions into the esophageal lumen, often in clusters. They give the impression that they might rupture at any moment. Although they appear to occlude the esophageal lumen they afford no obstruction to the esophagoscope. Usually a single varix is encountered first and towards the lower end of the esophagus two or more chains of varices may be located. An active bleeding point in a varix may be extremely difficult to localize and then only with persistence, great care, and patience. The locating of the bleeding point may be facilitated by first passing a Sengstaken-Blakemore triple lumen tube into the stomach. The gastric portion of the tube is filled with air and by pulling it up against the cardia firmly, the venous flow of the varices is reduced and thus the bleeding is lessened.

The management of esophageal varices may be considered from the standpoint of local treatment of the acute hemorrhage and the prophylactic treatment of varices.

During active bleeding, both supportive and local treatments are necessary and these include:

1) Transfusions
2) Local compression—balloon tamponade[22]
3) Intravenous pituitrin[21]
4) Injection of esophageal varices with sclerosing solution[17]
5) Emergency thoracotomy and ligation of varices[12]

The prophylactic treatments of varices include:

1) Injection with sclerosing solution[6,13-15,20,25]
2) Partial esophagogastrostomy[19]

3) Gastric transection[24]

4) Mediastinal packing[23]

5) Esophagectomy[5]

6) Intra-esophageal ligation of varices[7]

7) Ligation of periesophageal veins

8) Partial esophagogastrectomy and colon transplant[10]

9) Splenectomy

10) Splenic artery ligation

11) Hepatic artery ligation

12) Omentopexy[8]

13) Portacaval shunt[3] and

14) Splenorenal shunt.

The number and variety of procedures reported indicate that there is no completely satisfactory solution to the problem of hemorrhage from esophageal varices.

The treatment of esophageal varices by the injection of sclerosing agents through an esophagoscope was first described by Crafoord and Frenckner[6] in 1939, using quinine as the sclerosing agent. Moersch duplicated this procedure in 1940 using sodium morrhuate[14] and in 1941 reported eleven cases in which this technique was employed.[15] Since then satisfactory, in fact, even striking, results have been reported by several authors.[13,14,17,20,25] Patterson[18] has said: "To my knowledge, no other method has been proposed which can so effectively protect these patients bleeding from esophageal varices from recurrence of hematemesis." On the other hand, some authors have described this technique as being unsatisfactory, hazardous, and not justifiable.[2,11]

The ideal solution to the problem of portal hypertension would seem to be the establishment of an effective shunt between the portal and systemic venous beds. Two types of shunting procedures usually are performed to reduce portal hypertension. One is a splenorenal shunt, or anastomosis between the splenic and renal veins. The other is a portacaval shunt, or an anastomosis between the portal vein and the inferior vena cava. The latter diverts a larger volume than the splenorenal shunt, but quite frequently the portal vein is useless for anastomotic purposes because of pylephlebitis, multiple branching, or

other deformities. Unfortunately, in younger children especially, these are technically difficult or impossible. This applies particularly to the extrahepatic type of portal-venous obstruction where the portal vein is not available for shunting. Either one of these shunts may be unsuccessful because of thrombosis at the site of the anastomosis. Blakemore[3] in 1951 reported on 111 cases in which shunts were performed with a mortality of 16.2 per cent. Beckman has reported splenorenal shunts resulting in control of hemorrhage in 60 per cent of his cases. In our group it is felt that there is a far greater chance of success in accomplishing a satisfactory portacaval or splenorenal shunt in children over ten years of age. Consequently it has been our hope that hemorrhage from esophageal varices in younger children could be controlled by injection of the varices with sclerosing agents until the time arrived when a successful shunting operation could be performed.

The injection technique of treating esophageal varices was first used at the Hospital for Sick Children in Toronto in 1955. At this time the procedure became necessary in one little patient who was gradually bleeding to death in spite of previous surgery, and in spite of transfusions and balloon tamponade. The results were so gratifying in this particular individual that we were asked to continue to use this method of treatment on other patients with hemorrhaging esophageal varices.

## REPORT OF A CASE

A three and a half year old boy was first admitted to this hospital because of gross melena associated with an upper respiratory infection. He had had jaundice at birth although otherwise was well until the age of two and a half years when melena developed for which he received transfusions. Examination showed a malnourished boy who was pale and appeared chronically ill. Liver function tests were normal. An esophagogram at this time showed varices at the lower end of the esophagus. He subsequently had several admissions for treatment of melena or hematemesis and at the age of five years a portacaval shunt was attempted but was technically impossible because of an unsatisfactory portal vein to provide an anastomosis. The postoperative course was very stormy, complicated by a right pleural effusion, and he continued to have severe hematemesis. The hemorrhage was controlled only temporarily by the Sengstaken-Blakemore bag and many transfusions were necessary to keep up with the blood loss. His condition had now become so poor that the parents had lost hope and did not feel it was worth while trying anything else to save him. At this point

it was decided to attempt to stop the hemorrhage from the varices by injecting a sclerosing solution. Esophagoscopy revealed large varices beginning at the mid-esophagus and extending to the cardia. Three varices were injected with 5 per cent sodium morrhuate. He was transfused during the procedure and the next day his hemoglobin was 12 gms which was the highest that had been recorded at any time during his hospitalizations. Two further injection procedures were carried out at weekly intervals and he was then discharged from hospital. One month later he was readmitted for treatment of an acute upper respiratory infection and on this admission splenectomy and splenorenal anastomosis were performed. Portal vein pressure was taken before, during, and after the operation and showed no significant lowering of the portal pressure after the splenorenal anastomosis was established. Four months later he was readmitted with an upper respiratory infection and after this had subsided an adenotonsillectomy and esophagoscopy were carried out. There were no active varices present. He was free of symptoms for 19 months when he developed influenza and had some melena. In the interval he had been going to school and playing quite normally. Esophagoscopy on this admission revealed three small active varices which were injected with sodium morrhuate. Two months later he was admitted for reassessment and at this time esophagoscopy showed one small active varix which was injected with sotradecol. He was well on discharge. Four months later esophagoscopy revealed the esophagus to be essentially normal. For the past 15 months he has been leading a normal life and been free of any signs of bleeding. In view of the severity of the hemorrhage that occurred prior to the initiation of the injection of the varices, and that shunting procedures were not effective, we feel that the injection of sclerosing agents into the varices in this patient has resulted in a remarkable improvement in his clinical condition. How long he will be well remains to be seen.

Endotracheal anesthesia is used for the endoscopic procedures on the patients with esophageal varices. Although ether and other volatile anesthetics have been used on several occasions, we have found that combination of intravenous barbiturates and relaxants with nitrous oxide and oxygen by controlled respirations to be most satisfactory. Using the controlled respiration technique, the venous pressure within the varices is lowered and therefore hemorrhage from them is less of a problem than when the patient is breathing voluntarily. The esophagoscopes used in the treatment of esophageal varices need to be relatively large in diameter, not only to provide better visualization of the area concerned, but also to put the veins on the stretch and to help compress the veins after the injection has been

accomplished. A six mm Lell or Jackson esophagoscope, for example, can be used quite safely in a child of two years of age or more. We find that a built-in aspirating tube in the esophagoscope is most important to facilitate identification of the varices and especially to localize bleeding points when such are present. To find a bleeding point in the presence of varices can be most difficult and frustrating under the best of circumstances, but without constant aspiration it is almost hopeless. The varices can be made to dilate and become more prominent by the use of negative pressure through the esophagoscope. Thus the varices may be made to become apparent where otherwise they might escape one's notice.

We have found the Norris needle and clamp quite satisfactory for varices injection. The needle should not be more than 5 cm longer than the length of the esophagoscope being used and the tip of the needle must be long enough to see beyond its thicker shaft. The use of a rubber connection between the needle carrier and the syringe is of great value in preventing unnecessary movement of the needle during the injection.[25] Luer Lok connections may prevent the sclerosing solution from being sprayed into the eyes of the endoscopist as a result of the rubber tubing slipping off during the injection. For many of the patients in the series we used a 5 per cent solution of sodium morrhuate as the sclerosing agent. We also used ethanolamine oleate® for some of the injections but did not feel that it caused as rapid a sclerosing action as did the sodium morrhuate. Over the past few months we have been using sodium sotradecol® in a 3 per cent solution. We have found that this latter agent causes very little postoperative complications such as pain in the chest or abdomen, pleuritic reaction and fever. One patient had a rather severe pleural effusion following injection of sodium morrhuate and we suspect that the solution was injected outside the lumen of the vein in that particular instance. The same child subsequently required a ligation of the varices and the surgeons found it extremely difficult to perform the operation because of a rather marked periesophageal fibrosis. It is wise to keep a constant check on the pulse rate during the injection of the sclerosing solution and if there is any change of the cardiac rhythm, injection should be stopped in that particular varix at least.

Unless there is active hemorrhage we prefer to begin the injection in the most proximal varix in the esophagus. Under direct visualization through the esophagoscope, the needle point is introduced into the varix parallel to its medial wall and three to five cc of the sclerosing fluid is injected. If the needle is withdrawn from the varix without injecting the solution, the hemorrhage from that small needle

point can be exceedingly severe as we found to our chagrin on one occasion. In order to reassure ourselves as to whether or not the needle was in the lumen of the vein in the first few cases we injected diodrast and observed its course by fluoroscopy. When the varix is injected the needle is withdrawn and the esophagoscope immediately advanced so as to create pressure on the point injected. The next varix in turn is injected until the procedure is completed. We have made as many as six injections at one sitting. In our series it has taken as little as one or as many as eight injection procedures over a period of one year to achieve a good result.

There was a total of 15 patients in this series whose ages ranged from 23 months to 16 years at the time of the first injection. Thirteen of these patients had esophageal varices secondary to extrahepatic portal hypertension and two were secondary to intrahepatic portal obstruction.

Nine of these 15 patients achieved what we have considered to be good results in that they had no further blood-loss or the incidence of hemorrhage was greatly reduced, negative esophagoscopy, and were in general good health. These nine patients have been asymptomatic from one to three years from the time of last injection. One patient required only one injection, while three required two injections, two required four injections, two required seven injections, and one eight injections. All except one of these patients had a splenectomy prior to the endoscopic injection of esophageal varices. This one patient has been satisfactorily controlled by injection of the varices alone for 21 months. Seven of the nine patients had operations for splenorenal anastomosis or portacaval anastomosis or both. These were carried out before or during the course of the injections of the varices. However in four of these cases portacaval shunt was considered to be technically impossible at operation. One other patient in the fifteen was considered to be improved significantly by varices injection. She had had 53 admissions to hospital because of hemorrhage from the esophagus prior to the injection procedure, and after five injections she has bled intermittently but the episodes of bleeding have been much less frequent and much less severe.

Four of the patients in the series were considered to be failures in the respect that from four to nine injections of the varices failed to control the hemorrhage to any appreciable degree. Three of these subsequently required ligation of the varices. The fourth, with severe cirrhosis of the liver secondary to Wilson's disease, died of complications of surgery for portacaval anastomosis. In another

patient with cirrhosis an emergency injection of esophageal varices was carried out when the patient developed severe esophageal hemorrhage following a portacaval shunt. The hemorrhage was controlled by the injection although the patient died four days later in hepatic coma. It was interesting to find at autopsy that the varices that were injected were thrombosed.

We have been impressed by the number of times hemorrhages have occurred during a bout of upper respiratory infection, and in particular tonsillitis. We would therefore advocate adenotonsillectomy where indicated as a part of the management of those patients with esophageal varices.

In presenting this paper we are not advocating or suggesting that the injection of sclerosing agents in the esophageal varices is the only treatment. Rather it is a supplement to medical and surgical management. Once injections have been instituted they should be carried out regularly about once a week until no further varices are apparent. If too much time elapses between the injections, it has been our experience that the technique is not as successful. After the varices apparently have been controlled, the patient should be re-examined every six months whether or not there have been any symptoms of bleeding. It is much easier to control the varices when they are small, should they recur, than it is to eliminate the varices that have become extensive.

## SUMMARY AND CONCLUSIONS

There should be no doubt that in patients suffering from portal hypertension, the establishment of a satisfactory shunt between the portal and systemic veins should still remain the treatment of choice. However, it is our experience that the injection of esophageal varices with sclerosing solutions is a useful adjunct to other accepted methods of treatment for both the control of acute bleeding and the prevention of hemorrhages.

The injection technique we feel is particularly useful: 1) to control repeated bleeding in patients with advanced cirrhosis unsuitable for more extensive surgery; 2) for patients in whom shunting procedures have failed and they still continue to bleed; 3) to control acute bleeding where conservative measures are ineffective; 4) in the younger age groups shunting procedures, especially splenorenal shunts, are very often unsuccessful whereas these procedures have more hope of success when the patient is about ten years of age. With this in

mind we are trying also to keep these younger children from hemorrhages by repeated injections and save more definitive surgical procedures for later.

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# Abstracts of Current Articles

VICTOR R. ALFARO, M.D., ABSTRACT EDITOR

## EAR

### Measurement of Auditory Fatigue and Adaptation in Patients; the "Kietz-test" and its Clinical Significance

*Langenbeck, B.*: Zschr. Laryng. 38:202-211, 1959.

Dr. Langenbeck may be familiar to many readers as one of the many proponents of so-called "noise audiometry": the performance of audiometric tests in the presence of calibrated noise.

In the present paper, he reports on his efforts to take the measurement of auditory fatigue and adaptation out of the laboratory, where it has been studied for quite some time, and apply it to clinical testing. The instrument used consists of an electronic time switch (constructed by Dr. H. Kietz) which is connected to a noise audiometer (manufactured by Atlaswerke, Bremen, Germany). By means of the switch, the noise is periodically interrupted: 0.4 seconds "on," 0.04 seconds "off." The audiometric test tone is controlled independently from the noise channel and applied in the conventional manner. An audiogram taken with the aid of this instrument is referred to as the Kietz-test. Its results fall somewhere into the interval between the audiometric thresholds in quiet and in noise (the latter taken with the same noise level continuously "on"). At a 60 db noise level, for instance, the Kietz-test comes out approximately halfway between the quiet and the noise thresholds. The difference in level between the results of the Kietz-test and the ordinary noise audiogram is taken to indicate the amount of recovery ("re-adaptation") taking place during each silent interval. The test is said to be performed without difficulty by clinical patients.

In middle-ear deafness, the relation between the three thresholds is essentially unchanged. However, in some cases of inner-ear deafness, the results of the Kietz-test run very close to the standard noise audiogram, indicating a minimal recovery during the silent intervals.

The latter was observed to occur in cases of Ménière's disease (confined to the low frequencies) and immediately after an acoustic trauma. The suggestion is made in this respect that the test may be utilized to determine the state of "activity" as to repair and degeneration after acoustic trauma.

At the end, a schematic classification is presented of the various effects of experimental, short-time noise exposure upon the recovery curve: (a) rapid recovery (normal); (b) various degrees of delayed recovery (pathologic); (c) a decay of the recovery curve below the level of the expected masking threshold followed by delayed recovery. The latter has been referred to by the author at previous occasions as the result of "micro-trauma" to the inner ear.

TONNDORF

**Surgery of the Vestibular Window**

*Muendnich, K.*: Zschr. Laryng. 38:131-157, 1959.

This lengthy article summarizes the present state of our knowledge concerning Fenestration, Mobilization, their modifications and sequelae. Because of its own condensed nature, it does not lend itself very easily to reviewing. However, a few worthwhile points can be brought out. The bibliography contains the names of 77 authors, many of them with multiple references. Although 80% of those are Europeans (including British authors), the list contains 16 American names which are frequently referred to in the text. This latter fact distinguishes the paper from many of our own contemporary efforts which if foreign literature is considered at all confine themselves largely to papers published in English (J. Laryng. and the Acta [Stockh.]). The difference becomes even more obvious when one analyzes in which language the different papers are published of which there is a total of 117: English (44), French (19), German (47), Italian (6), Swedish (1).

The simplest way of describing the content of the present paper is by giving a list of the chapter headings, many of them phrased as questions: (1a) The Significance of Penetration of the Vestibular Window with Reference to Perilymphatic Drainage. (1b) The Closure of the Window. (2) Does the Footplate Fenestration, without Mobilization or Stapes Extirpation, Produce an Improvement in Hearing, even when an Intact Eardrum is Present? (3) Is It Advisable to Combine Vestibular Fenestration and Stapes Mobilization? (4a)

What is the Effect of Vestibular Surgery upon Tinnitus? (4b) What is the Effect of Vestibular Surgery upon Vertigo? (5) What is the Danger of Complications after Surgery? (5a) Surgical Indications and (b) Technical-Surgical Considerations.

In reading the article, this reviewer was impressed with the volume of publications, the diversity of approaches discussed, and the heated argumentation pro and con concerning vestibular surgery as described in this article. The paper is a valuable source of references, compiled in a critical form, for anyone interested in modern ear surgery.

TONNDORF

**A New Concept Regarding the Limit of the Labyrinthine Function**

*Kurata, T.*: J. Oto-rhino-laryng. Soc. Japan 61:1583 (Oct.) 1958.

The author used rabbits and guinea pigs on which so-called subliminal rotation with angular acceleration of 1.0° and 0.3°/sec$^2$ was imposed. From the series of experiments the author concluded as follows:

The critical angular velocity which induces maximum jerks will be called "the limit of pure optic nystagmus." Similar changes of nystagmus were observed when subliminal rotation was imposed on the animal with intact vision, and the frequency of jerks showed a peak at a certain angular velocity, which, however, was by far faster than that in pure optic nystagmus and will be called "the limit of the labyrinthine function."

HARA-KUROZUMI

**Changes of Capillary Blood Vessels of the Middle and Inner Ears in Cases of Experimental Otitis Media**

*Kikuchi, T.*: J. Oto-rhino-laryn. Society, Japan, 61:1757 (Nov.) 1958.

In the first part of the article, the distribution of capillaries in the middle and inner ears of the rabbit is described. The author summarized it as follows:

1) The major blood vessels supplying the malleus and incus coursed on the ligaments attached to both ossicles.

2) The intermediate zone of the ear drum had a broad area which showed no blood vessels at all.

3) Dense anastomosis was seen between the capillaries of the external ear and those of the middle ear.

4) The capillaries in the various parts of the inner ear, such as the stria vascularis, macula and crista acustica were studied and no communication was found between the blood vessels of the middle ear and those of the inner ear.

In the second part of the article, changes of capillary nets in the ear in which otitis media was induced by injection of streptococcus aureus or 3% silver nitrate solution were observed. The conclusions were summarized as follows:

1) Capillaries of the tympanic cavity increased rapidly in number in the early stage of the inflammation and kept increasing even in the late stage.

2) At the initial stage, the caliber of the newly-grown vessels was so fine as to be difficult to get India ink into them. The caliber grew larger and finally became as large as that of the ordinary capillary network.

3) The caliber of venules grew more rapidly than that of arterioles.

4) In the present series of the experiment, no remarkable changes of vessels nor newly-formed vessels were found in the ossicles themselves, but granulation tissue was found much more frequently on the surface of the malleus than on the incus, followed by the round window and the ear drum in descending order.

5) Increasing numbers of the newly-formed vessels around the round window seemed to suggest that spread of inflammation to the inner ear was likely to be through the round window.

A number of photographs of the capillaries injected with India ink were presented.

HARA-KUROZUMI

**Endaural Tympanic Approach to the Facial Nerve**

*Muerman, O. W.*: Acta Oto-laryngologica 49-6 (Nov.-Dec.) 1958.

The author exposes the facial nerve via the middle ear using the technique of the stapes mobilization operation. The nerve is exposed from above the oval window to the stylomastoid foramen, using burr and gouge, without opening the mastoid cells or endangering the ossicular chain. Three case reports are included.

HILL

**Paracusis Willisii**

*Gundersen, T.*: Acta Oto-laryngologica 49-6 (Nov.-Dec.) 1958.

Studies, using pure tone and speech audiometry in high and low frequency background noise, were carried out on 16 patients with paracusis Willisii. These showed no actual improvement in the hearing threshold, the masking effect being the same as in patients with normal hearing and there being no difference in high or low frequency noise. Any apparent improvement in hearing is due to the normal hearing person raising his voice in the presence of noise. Patients with perceptive deafness may have paracusis Willisii. Good cochlear function is necessary to produce the symptoms of paracusis. The author concludes that this technique of noise audiometry is of value in investigating cochlear function.

HILL

**Static or Kinetic Labyrinthine Reflex**

*Fukuda, Hinuki,* and *Tokita*: Acta Oto-laryngologica 49-6 (Nov.-Dec.) 1958.

Using the Barany technique two blindfolded leghorn hens were rotated 100 times in 200 seconds to both sides daily for two weeks. As a result of repeated rotation the authors noted a decrease in post-rotatory nystagmus which could not be explained by fatigue, damage or paresis. They conclude that the improvement in equilibrating function is due to formation of what they designate as a kinetic labyrinthine reflex.

HILL

**Uber Die Ursache Der Progressiven Altersschwerhorigkeit (Presbycusis)**

*Sercer, Von A.*, and *Krmpotic, J.*: Zagrer, Jugoslavia. Acta Oto-laryngologica, Supplement 143.

A monograph of some 32 pages in German, dealing with the problem of etiology of presbycusis. The authors advance the hypothesis that hyperostosis in the internal auditory meatus, occurring as a part of the aging process, on the inner surfaces of the bones of the skull is the primary cause. The incidence and extent of these bony changes in the internal auditory meatus vary, depending upon the general condition of the individual. They are most evident in basal coil where they gradually invade the tractus spirales and crush the nerve fibers. This is considered to be primary and loss of the ganglionic cells secondary. Impairment of hearing due to arterio-sclerosis, hormonal influences, or pathological changes in the middle ear are only coincidental, although possibly adding to the loss.

HILL

**A Study of Bone Conduction Hearing During the Periodical Changes of Meatal Pressure in Reference to Clinical Practice (A New Interpretation of Géllé's Test)**

*Nakashima, R.*: J. Oto-rhino-laryng. Soc. Japan. 61:1602-1613 (Oct.) 1958.

The well-known Géllé's test for the diagnosis of otosclerosis has been interpreted from a new point of view, and a new test method has been developed that is more sensitive and simpler than previous one.

The apparatus consists of audiometer, manometer and Politzer's balloon.

The procedure of the test is as follows:

The bone conduction sound of 250-4000 cps, 40 db above threshold is imparted to the ear to be tested, then the pressure of the external auditory canal is changed periodically by pressing Politzer's balloon twice a second. The pressure is gradually increased and when the bone conduction tone starts to pulsate the pressure is measured by the manometer.

The results obtained with various types of deafness were as follows:

1) The pressure was below 5 mm Hg in those of normal hearing and perceptive deafness.

2) The pressure was above 60 mm Hg in otosclerosis.

3) In the case of other conductive deafness the pressure was 10-60 mm Hg regardless of the presence of drum perforation.

The pulsation of the bone conducted tone in this method has been proved by experiments on the living human ear to be due to the distortion of the inner ear.

This new method, the mechanism of which is fundamentally different from the usual modified Gelle test, has been designated by the author as "dynamic Gelle test." The original Gelle test must be a kind of this dynamic method.

HARA

## THROAT

**Vibratory Patterns of Vocal Cords in Laryngeal Paralysis (Paramedian and Intermediary Positions)**

*Jeschek, J.*: Zschr. Laryng. 38:346-354, 1959.

Analysis of high-speed motion pictures shows that paralyzed cords move in various modes and to different degrees. If the (paralyzed) cord is in the paramedian position and is very stiff, its amplitude of vibration is small. With lesser stiffness, vibrations become wider but remain confined to the free rim which moves dominantly in a vertical plane. When the cord is extremely flaccid, its amplitude becomes very large, hitting the lateral wall during one phase and even forcing the unparalyzed cord over during the opposite phase (so-called "alternating" vibration).

Another case is described with bilateral paralysis and unilateral arypexy. In spite of differences in the elastic properties of both cords, motion was bilaterally synchronized.

In a further case (unilateral paresis, intermediary position) two modes of motion were observed. At one time, the paralyzed cord made large, flaccid motions, "like the vibrations of a rope." The two cords were not synchronized. At other times, the cord made minimal

motions of its free rim. (Nothing is said about synchronization in the second mode.)

The author reasons that the malfunction of a paralyzed larynx has two causes: (1) the alteration of the aero-dynamic properties and (2) the alteration of the elastic properties of the cord. The first of these causes is demonstrated from laryngeal kymograms which show structural alteration of the pathway. The second cause, according to experiments by the author, is aggravated by failure of the adductor muscles.

However, the most interesting conclusions are not stated in the paper. Therefore, the reviewer may be permitted to add them here: Evidence is presented that paralyzed cords vibrate, although in an abnormal manner. Since the latter is traced to missing muscular action, the paper serves to support the classical aero-dynamic theory of laryngeal function: Vibration of the vocal cords in phonation is caused aero-dynamically; the muscular action is needed only for proper positioning of the cords. This evidence does not favor the neuro-chronaxic theory of Husson.

TONNDORF

**Clinical and Surgical Problems of Cancer of the Larynx and Hypopharynx**

*Pietrantoni, L.*, and *Fior, R.*: Acta Oto-laryngologica, Supplement 142.

A carefully done analysis of 570 consecutive cases operated upon in the Ear, Nose and Throat Clinic of the University of Milan between 1948 and 1954. Their classifications of cases, adopted from the Unio-Inter-Nationalis contra Cancrum, were as follows:

Stage 1. Superficial tumor: no impairment of motility or palpable nodes.

Stage 2. Infiltrating tumor: impaired motility, no palpable nodes.

Stage 3. Tumor extending to more than one laryngeal or hypopharyngeal region, or Stage 1 or 2 with histological metastases, or with palpable movable nodes.

Stage 4. Extrinsic tumor or Stage 1, 2, or 3 with fixed nodes or distant metastases.

While the use of tobacco was considered as a cancerogenic factor, only local irritative effect could be attributed to the use of alcohol. All except 48 cases were reported as squamous cell carcinoma. These were divided simply into differentiated and poorly differentiated groups. From their studies the authors believe that radical surgery of the anaplastic tumors offers favorable prognoses, if combined with neck dissection.

Great stress was placed upon thorough pre-operative study and preparation, and postoperative care, with special attention to nutrition and protective antibiosis.

Indications for the various types of operation as well as the author's technique are given. Combined neck dissection and laryngectomy is advocated for all hypopharyngeal and subglottic neoplasms with special consideration to the dissection of the posterior branch of the spinal accessory nerve. In cases involving bilateral neck dissection the authors now elect to dissect the contralateral vein from its sheath, preserving it, in order to avoid the possible sequelae from inadequate venous return. En bloc removal is carried out, working from above downward. Their operative and postoperative mortality in all types of cases was 2.7%. Distant metastases were only 4.15%.

Careful attention is paid to functional rehabilitation. Seventy-six per cent of the patients were able to resume their previous occupations.

HILL

## LARYNX

### A Case of Aberrant Parathyroid Gland Tumor Found in the Lateral Pharyngeal Wall

*Funayama, N.*: Oto-Rhino and Laryngological Clinic, Kyoto, 51:664 (Aug.) 1958.

The first case of aberrant parathyroid tumor was recorded by Hickmann in 1869. Since then a number of cases have been reported in literature. Funayama added another case. The patient was a 50 year old male. He developed a swelling in the right palatine tonsil which appeared not unlike a peritonsillar abscess. No pus was seen when the incision was made by another surgeon.

The patient consulted the author who diagnosed it to be a benign tumor of the right tonsil and excision was performed. Bleed-

ing was so profuse during the operation that ligation of the external carotid artery was performed. The tumor removed weighed 70 grams. The histopathological report was parathyroid gland tumor which had become malignant. The patient is now receiving a series of x-ray treatments.

HARA-KUROZUMI

**Associated Carcinoma of Larynx and Lung**

*Rubenstein, Alan S., Graham, James* and *Barnes, Neale*: A.M.A. Arch. Otolaryng. 68:710-714 (Dec.) 1958.

The authors review the literature reporting associated carcinoma of larynx and lung, referring to one study which described 12 patients and another 19; and a third study reported an amazingly high incidence of associated lung and laryngeal cancer—5 out of 20 patients with laryngeal cancer were found at autopsy to have concurrent or subsequent bronchial carcinomas.

The authors report two cases of associated carcinomas of larynx and lung, one concurrent, the other consecutive. Case 1 was a white man 66 years of age, treated in 1944 for carcinoma of the vocal cords, who in 1951 suddenly developed symptoms resembling bronchial asthma. Thoracotomy in 1952 revealed a well-outlined mass near the lateral aspect of the hilus of the middle lobe. Right middle lobectomy was performed; epidermoid carcinoma was found histologically. The association here was consecutive. In Case 2 it was concurrent. When first seen on March 16, 1957, a 62 year old Negro (male) complained of hoarseness and a constricting retrosternal feeling on exertion. Subsequent laryngoscopy and biopsy revealed grade II to III epidermoid carcinoma from the left vocal cord. Bronchoscopy disclosed a lesion at the orifice of the right upper lobe bronchus; biopsy of the lesion showed epidermoid carcinoma of the bronchus, grade III.

The subject of multiple primary neoplasia is briefly reviewed and the interesting comment of Warren and Gates is pointed out, that the tendency for a person to develop a second cancer is 11 times greater than that of the individual without a previous cancer. In a series of 2829 autopsies on cancer patients they found 194 (6.8%) instances of multiple primary malignancy. Rubenstein et al. state that there is a tendency for multiple primary cancers to occur in the same organ or in paired organs. The highest incidence in paired organs, in order, is in breasts, ovaries, testicles and kidneys.

In treating patients having two concurrent carcinomas, the more lethal lesion should be attacked first.

The authors caution that patients having carcinoma of the larynx should be carefully observed for the appearance of carcinoma of the lung.

HILDING

## MISCELLANEOUS

### Sinography, Especially with Reference to Block Dissection of the Neck

*Frenckner, Paul*: Acta Oto-laryngologica 49-4 (July-Aug.) 1958.

Because of the possibility of anomalies of the cranial venous pathways bilateral resection of the internal jugular veins may have unfortunate sequelae. Therefore, the capacity for venous return should be determined before surgery. The technique of sinography, originally developed to differentiate the involved side in cases of sinus thrombosis in cases of bilateral mastoiditis, involves the exposure by trephining over the posterior position of the longitudinal sinus and the injection of contrast medium with coincident roentgenographic studies. This has been carried out routinely prior to block dissection by the author who then has adapted his procedure accordingly. In 50 per cent of 30 sinographies, total or nearly total aplasia was found on one side.

These studies have been correlated with earlier anatomical and roentgenological studies showing fairly consistent findings with the size of the jugular foramen.

The significance of this contribution should be obvious. While the author does not imply that sinography be routine, his statement that "the capacity of the venous return on either side should be elucidated" certainly has validity and at least roentgenographic study of the jugular foramina might well be indicated. The number of cases showing aplasia seems excessively high but these were in the group undergoing sinography. It could be assumed that there were findings indicating special attention to this group, possibly as a result of roentgenography of the jugular foramen.

HILL

**Clinical Quantitative Gustometry**

*Hinchcliffe, H.*: Acta Oto-laryngologica 49-6 (Nov.-Dec.) 1958.

This test employs the Beebe-Center standards using the gust scale for measuring subjective taste strength. Dilutions of sucrose, quinine, tartaric acid, and sodium chloride are used with addition of −0.25 log gusts for each taste quality. The dropper technique was followed using tap water as the solvent. As a result of his observations on a random sample of population the author considers the test valuable and reliable.

HILL

**Clinical Study on the Tonsillar Focal Infections**

*Kimura, T.*: J. Oto-rhino-laryng. Soc. Japan. 61:1672 (Oct.) 1958.

Forty-five cases of tonsillar focal infection were studied in comparison with 80 cases of tonsils without focal infections. The results were as follows:

1) Recurrent palatine tonsillitis was seen in the majority of tonsillar focal infection.

2) The palatine tonsils were usually buried and the superior tonsillar fossa was filled with pus or plug.

3) Fever, accelerated blood sedimentation rate, myocardial disturbance, decrease in albumin and increase in γ-globulin of the blood plasma protein were characteristic.

4) Focus provocation test by ultra-short-wave was reliable.

5) Antistreptolysin reaction showed much significance for diagnosis and prognosis of focal infection.

6) In surgically removed tonsils Streptococcus hemolyticus was demonstrated in 51.5%, Streptococcus viridans in 42.4%, and staphylococcus in 22.7%.

HARA-TSUGAWA

**The Influence of Proprioceptive Stimuli upon Prerotatory and Postrotatory Nystagmus**

*Ichikawa, H.*: J. Oto-rhino-laryng. Soc. Japan. 61:1573-1577 (Oct.) 1958.

Without covering their eyes, five leghorns were rotated at two different postures and both perrotatory and postrotatory head nystagmus were observed. Constant optic stimuli were given to the animals during the rotation by rotating the revolving chair in the center of a large cylinder. The animals at the posture on a perch grasping it with their claws showed more jerks of perrotatoric head nystagmus but less jerks of postrotatory head nystagmus compared with those at the posture crouching on the flat plate of the revolving chair. Namely, the proprioceptive stimuli from the animal's legs to grasp a perch with their claws promote perrotatoric head nystagmus but decrease postrotatory head nystagmus.

HARA

**Osteomyelitis of the Mandible Following Irradiation**

*Ng, Elmer; Chambers, Jr., Frank W.; Ogden, Harry S.; Coggs, Granville C.; Crane Jackson T.*: Radiol. 72:1:68-74 (Jan.) 1959.

In an experimental study with dogs these authors demonstrated that removal of teeth prior to irradiation of the mandible within the therapeutic dose range significantly decreased the incidence of osteomyelitis. Mongrel dogs were used. A generally applicable method for this type of irradiation and the irradiation technique is described.

Gingival ulceration and osteomyelitis of the underlying mandible occurred following exposure to irradiation of 4000 "r'" (air) or more, under the conditions of this experiment. Osteomyelitis was not observed in the absence of ulceration of the overlying gingiva. Bone necrosis without osteomyelitis was not observed with the dosage and time range studied.

Nine photographs of extirpated mandibles demonstrate gross changes of mucosa and bone. Six photomicrographs demonstrate histologic changes. Two tables and 5 references are included.

JORSTAD

# Notices

## CASSELBERRY PRIZE

A sufficient fund having accrued from the Casselberry Fund for encouraging advancement in the art and science of Laryngology and Rhinology, this sum is now available in part or as a whole, for a prize award. Theses must be in the hands of the Secretary of the American Laryngological Association prior to January 1 of any given year.

The Award is a prize of money with accompanying certificate signed by the officers of the American Laryngological Association. The sum of money will be agreed upon by the Council of the Association after the manuscript has been evaluated by the Award Committee. It may be awarded in whole or in part among several contestants.

Eligible contestants may be: 1. Hospital interns, residents, or graduate students in Rhinology and Laryngology; 2. An individual with an M.D. degree who is actively practicing or teaching Rhinology and Laryngology in the Americas; 3. Any scientific worker in the field of Rhinology and Laryngology.

Manuscripts shall be presented to the Secretary of the Association under nom de plume which shall in no way indicate the author's identity. There shall also be a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant which the Secretary shall keep in his possession.

Manuscripts must be limited to 5000 words and must be typewritten in double spacing on one side of the sheet. The thesis shall not have been published elsewhere before submission.

The successful thesis shall become the property of the American Laryngological Association but this provision shall in no way interfere with publication of the thesis in the Journal of the author's choice. Unsuccessful contributions will be returned promptly to their authors.

The Award which will be made at the Annual Meeting of the American Laryngological Association shall be based on:

1. Originality of material.
2. Scientific and clinical value.
3. Suitability for this Award.
4. Method of presentation as to style, illustrations and references.

The maximum amount of the Award shall not exceed $200.00.

Lyman G. Richards, Secy.
Massachusetts Institute of Technology
Cambridge 39, Mass.

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## ACADEMY HOME STUDY COURSES

The 1959-1960 Home Study Courses in the Basic sciences related to ophthalmology and otolaryngology, which are offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months. Detailed information and application forms can be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 15 Second Street S. W., Rochester, Minnesota. Registrations should be completed before August 15.

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## ANNALS

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